PROGRESS REPORT ON ATOMIC ENERGY RESEARCH

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MAIN
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HEARINGS

BEFORE THE

SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT

OF THE

JOINT COMMITTEE ON ATOMIC ENERGY

CONGRESS OF THE UNITED STATES

EIGHTY-FOURTH CONGRESS

SECOND SESSION

ON

PROGRESS REPORT ON ATOMIC ENERGY RESEARCH IN MEDICINE, BIOLOGY, AGRICULTURE, AND FOOD PRESERVATION

JUNE 4, 5, 6, 7, AND 8, 1956

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PROGRESS REPORT ON RESEARCH

MONDAY, JUNE 4, 1956

CONGRESS OF THE UNITED STATES,
SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT
OF THE JOINT COMMITTEE ON ATOMIC ENERGY,
Washington, D. C.

The subcommittee met at 10 a. m., pursuant to call, in room P-63, the Capitol, Representative Melvin Price (chairman of the subcommittee) presiding.

Present: Senator Bricker, Representatives Price and Van Zandt.

Representative PRICE. The committee will be in order.

This marks the first of a series of open hearings by the Research and Development Subcommittee of the Joint Committee on Atomic Energy for the purpose of receiving progress reports on research work being done under Atomic Energy Commission contracts in the fields of medicine, biology and agriculture.

A similar series of reports given to this committee two years ago were most informative and were received by this committee and the public with great interest.

The results of this kind of research has been and will continue to be of valuable benefit to mankind. The work of such men as these, using the newly found research tools of atomic energy, will prove that the beneficent side of the atom will far outweigh its military side.

The committee appreciates you gentlemen taking time out from your laboratories all over the country to come here this week to give us your reports. Through the cooperation of Dr. Charles Dunham, Director of the AEC Division of Biology and Medicine, and his assistants, this group of outstanding scientists from various parts of the country has been assembled.

The committee appreciates your assistance, Dr. Dunham. If you are ready, will you please proceed with the program you have worked out and introduce the speakers?

STATEMENT OF DR. C. L. DUNHAM, DIRECTOR, DIVISION OF BIOLOGY AND MEDICINE, UNITED STATES ATOMIC ENERGY COMMISSION

Dr. DUNHAM. Thank you, Mr. Chairman. It is a genuine privilege to have been asked to bring before your subcommittee a group of distinguished scientists eminently qualified to describe to you some of the exciting developments which are taking place today in the fields of medicine and agriculture because of the ready availability in the United States of the tools and the byproducts of atomic energy.

These accomplishments bear witness to the wisdom and foresight of the Congress, and especially of the Joint Committee on Atomic

Energy in insisting that those who administer this country's atomic-energy program keep constantly in mind the importance of utilizing atomic energy and its byproducts for the welfare of the Nation as a whole.

Two years ago I was privileged to plan for your subcommittee a series of hearings on the impact of atomic energy on the medical sciences. The material presented at the 1954 hearings on medicine as well as those on agriculture was drawn largely from the activities of AEC laboratories.

The speakers for the hearings which begin today will bring you up to date on significant developments in those fields of science, and in order that you can fully appreciate how atomic-energy techniques are being taken advantage of by medical and agricultural scientists all over the country, not just by scientists in AEC laboratories, we have prevailed upon a number of research leaders from American universities, medical schools, agriculture schools and foundations, as well as scientists from the Department of Agriculture and from the National Institutes of Health, to come here and tell you what atomic energy and its byproducts have meant to the advancement of their particular fields of interest.

As these hearings proceed, it will become increasingly apparent that atomic energy has an important contribution to make to almost every aspect of medicine and agriculture. In one form or another it is accelerating the advancement of knowledge of how to control disease.

Radioisotopes and radiations from reactors are being used to treat disease. Radioisotopes are contributing more and more to the art of diagnosis, and most important of all in the long run, radioisotopes are proving the open sesame for those who study the nature and causation of disease.

Similarly, in the agricultural sciences, radioisotopes and atomic radiations are making increasingly important contributions to our understanding of plant and animal nutrition, to the science of plant breeding, to the control of insect pests, to our knowledge of soil utilization, and to the advancement of the technology of food preservation.

We in the Division of Biology and Medicine of the Atomic Energy Commission are extremely proud of the part that we have been privileged to play in stimulating and encouraging these accomplishments in our role as administrators of the AEC's research program in biology and medicine.

This program encompasses more than 450 research projects at some 200 State and private institutions, in addition to the program of the AEC laboratories. It cannot be emphasized too strongly, however, that without the enthusiastic efforts of the scientists working in their laboratories and hospitals and in the fields and experiment stations, our efforts would have borne very little fruit.

I am firmly convinced that what has been accomplished to date is but a small beginning, and that there is scarcely any limit to what can be accomplished in the future if the country will continue to provide opportunities for the training of young scientists, facilities where they can work, and in terms of the national income, relatively modest sums to defray the costs of carrying out the research.

The first scientist which I wish to have present material to you is Dr. Richard C. Caldecott. He is a geneticist in the Field Corps Research Branch, ARS, United States Department of Agriculture, and

associate professor of agronomy and plant genetics department, University of Minnesota.

He is going to talk about the impact of radiation genetics on plant breeding.

Representative PRICE. Thank you very much.

Dr. Caldecott?

STATEMENT OF DR. RICHARD S. CALDECOTT, GENETICIST, FIELD CROPS RESEARCH BRANCH, AGRICULTURE RESEARCH SERVICE, UNITED STATES DEPARTMENT OF AGRICULTURE

Dr. CALDECOTT. It was with a great deal of pleasure that I accepted this invitation to appear before you and discuss the role of radiation genetics in plant breeding, because it seems that the time is ripe for a rational appraisal of where we are, how we got there, and what the future holds.

In order that we may start from a common point, let us look briefly at the basic materials with which a plant breeder works. We all know that the distinguishing characteristics of a wheat plant or of an animal or any other living organism, for that matter, are determined by the interaction in a suitable environment of heritable units called genes.

These genes are located within the chromosomes of cells and are distributed from generation to generation in a precise and orderly fashion. The plant breeder's object is to combine in new varieties those genes which result in a plant having the greatest number of desirable characteristics so that it can be of maximum utility to man.

The fact that is most apparent to the naturalist and until recently most disconcerting and frustrating to the geneticist and plant breeder, is the constancy or stability of any particular species; that is, in a natural environment species tend to mutate, produce new types of genes very rarely. Thus, the breeder doesn't have as many gene types to work with as he would like, because, remember, it is variability that makes the plant breeder's job possible.

It was of tremendous significance, therefore, when H. J. Muller and L. J. Stadler demonstrated in 1927 and 1928 that X-rays could be used to induce genetic changes in fruitflies and barley seeds. Further studies in the 1930's demonstrated that ultraviolet light induced genetic changes and, since the advent of controlled atomic fission, it has been shown that fast and slow neutrons can also produce mutations.

Thus, we now have a wide spectrum of radiations which can induce variation in the genetic materials of an organism. Let us now spend a moment or two on a comparison of the mutation producing potential of a few different sources of radiation because this is paramount in their productive use by plant breeders.

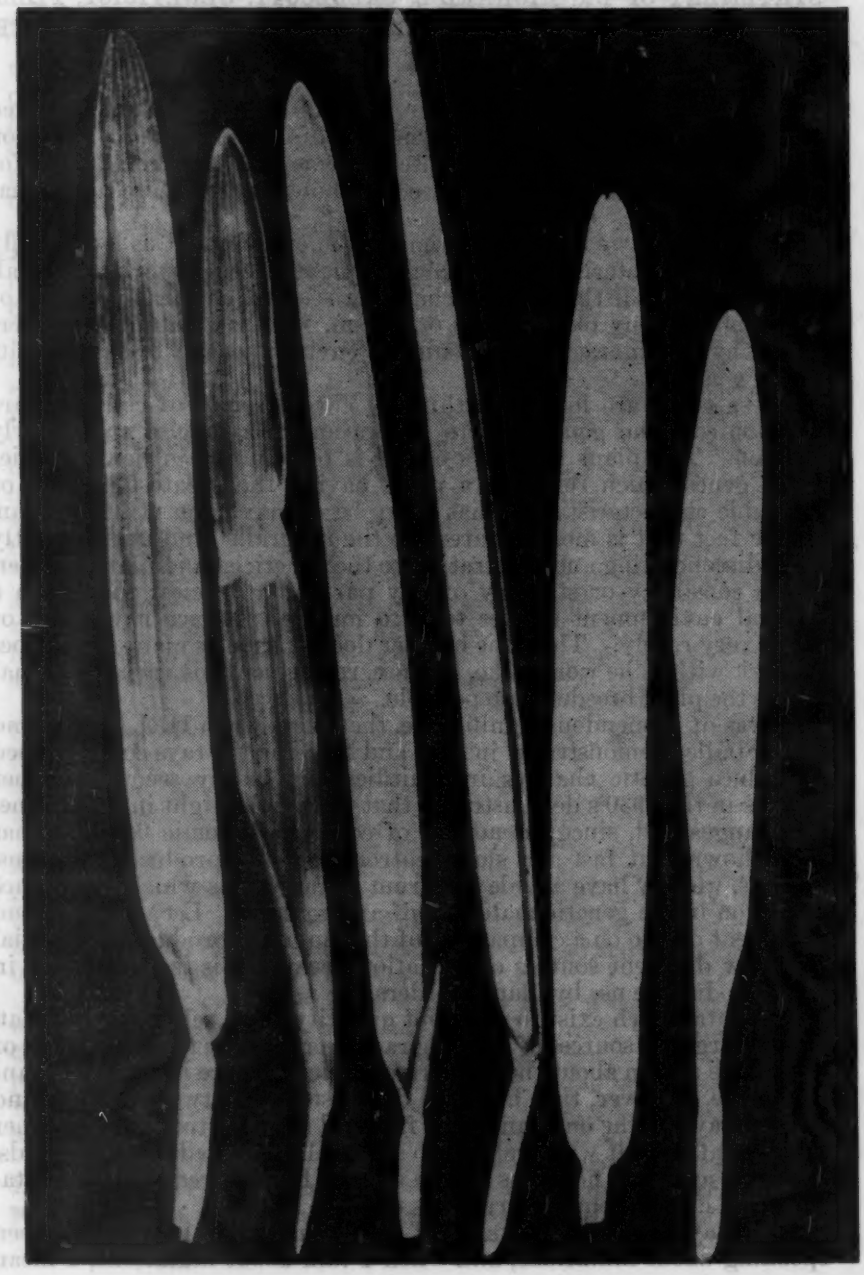
The data which exist in sufficient quantity to be reliable show that, by and large, all sources of ionizing radiations induce the same kinds of mutations and in about the same frequencies. There is one important difference, however, that has been demonstrated between X-rays and gamma rays on the one hand, and fast and slow neutrons on the other hand; that is, that when related to survival of treated dormant seeds, both fast and slow neutrons induce a much higher frequency of mutations and chromosomal aberrations than do X-rays.

If I may have the first slide, I will illustrate this. I have been speaking about mutations, and when I talk about mutations, I mean

a change that comes about in the plant that may be harmful or beneficial to the plant, and it is manifested in the different characteristics that the plant expresses when it grows.

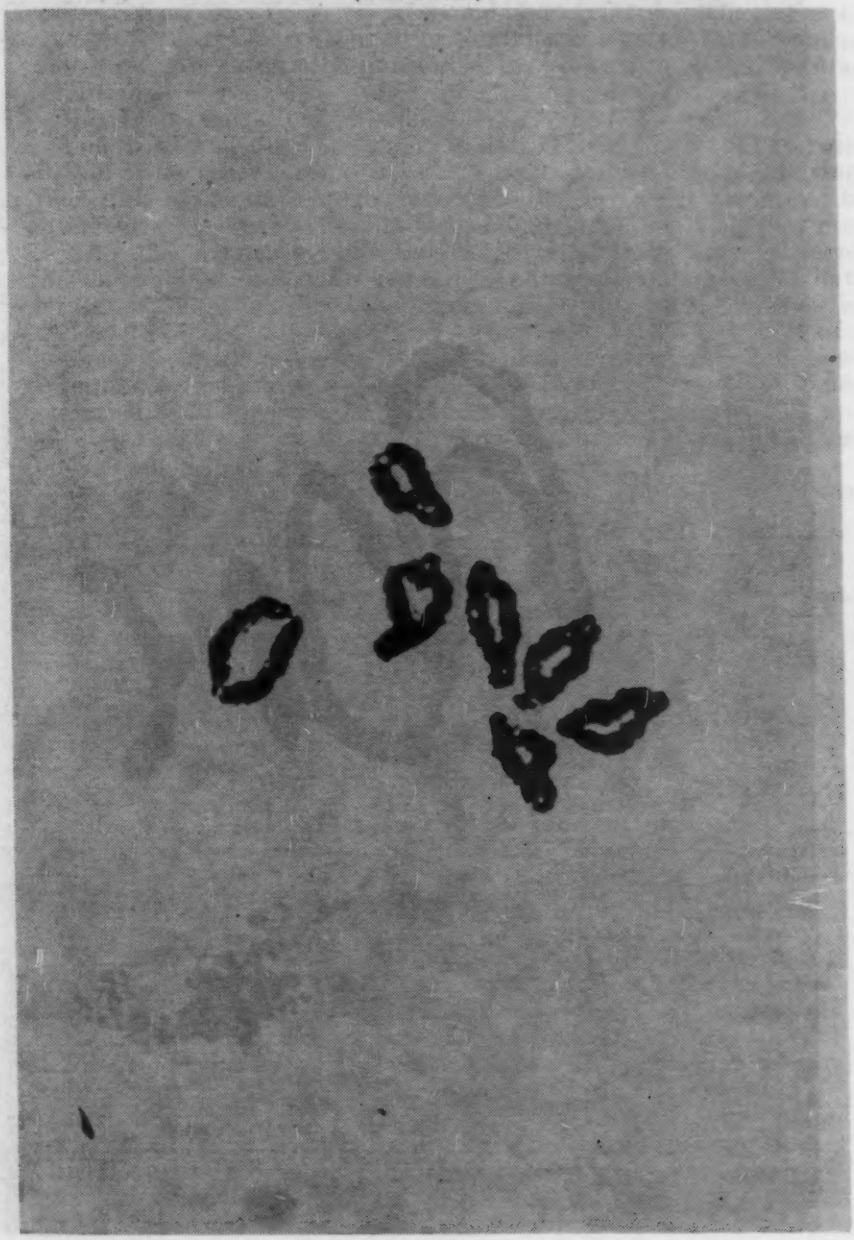
This is a normal leaf (exhibit 1). You see the changes that we can pick up. All of these particular changes we are looking at now would be what we would call deleterious or harmful to the plant, but the fact

EXHIBIT 1.—Mutant types in barley seedlings resulting from X-radiation.



remains that there is positive correlation between the production of this type of change and the production of beneficial changes. Thus, it is a perfectly satisfactory means of analyzing the material, that is to irradiate it and look for the changes which occur more commonly and determine their relative frequencies and then say that from this type of radiation we should be able to get a certain type or frequency of desirable genetic change.

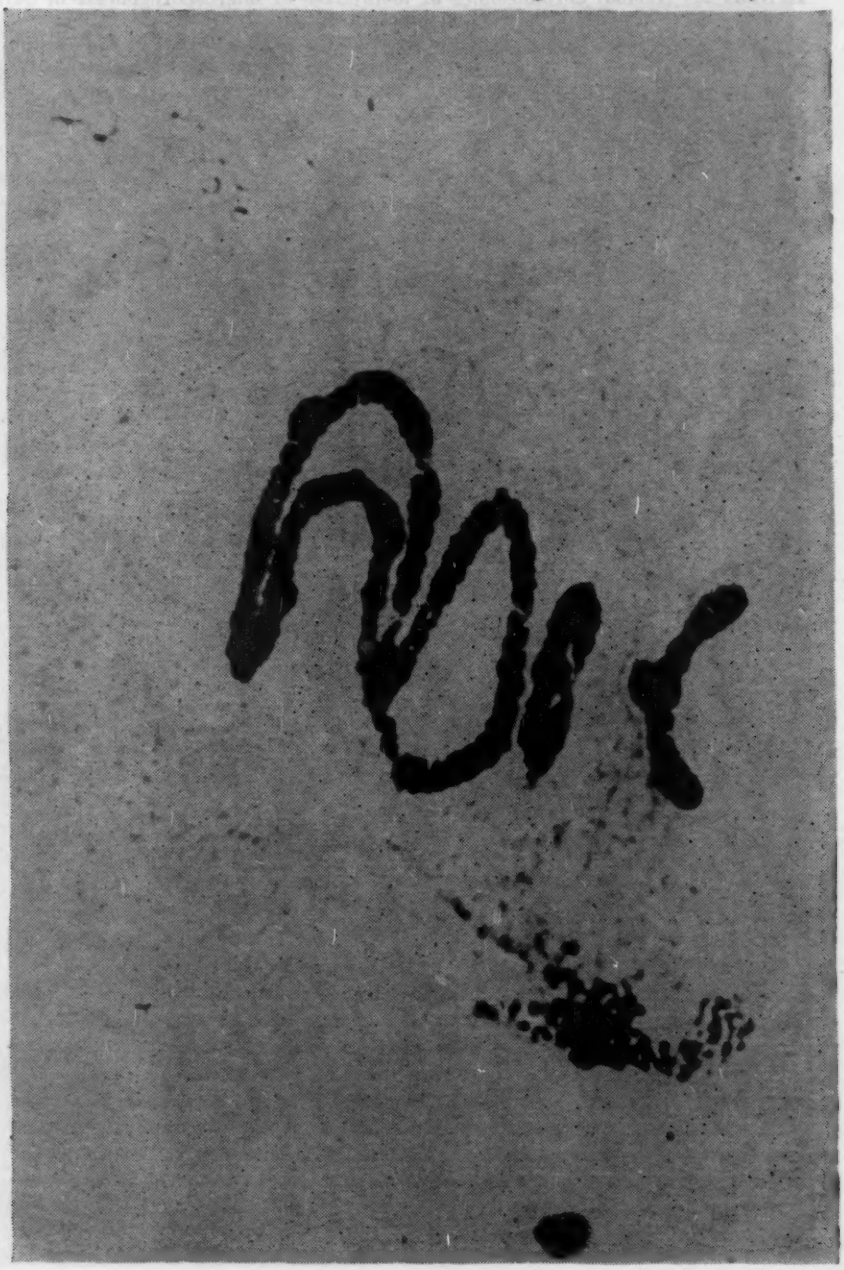
EXHIBIT 2.—Normal chromosomes at metaphase of microsporogenesis in barley (7 bivalents).



May I have the next slide?

I pointed out to you some of the types of mutation that occur. These involve a change on one of these chromosomes. These happen to be chromosomes in barley. The mutation then, to us, involves a change that doesn't apparently modify the visible structural characteristics of the chromosome (exhibit 2).

EXHIBIT 3.—Chromosomes at microsporogenesis in barley following thermal neutron irradiation (2 bivalents and 1 ring-of-10 chromosomes).



That is mutation as we distinguish from the chromosome break. The reason I want to make it clear is that they are both very important to the plant breeder in making maximum utility of ionizing radiations. Notice, there are seven of these little groups in this slide.

Representative PRICE. Could I ask you this question? Would you make these same experiments under normal research procedures?

Dr. CALDECOTT. These experiments would be impossible without radiation.

Representative PRICE. Impossible without radiation?

Dr. CALDECOTT. Yes, sir. I should modify that. The types of changes we are talking about occur so rarely in a natural environment that they are essentially impossible to work with under natural conditions.

May I have the next slide (exhibit 3)?

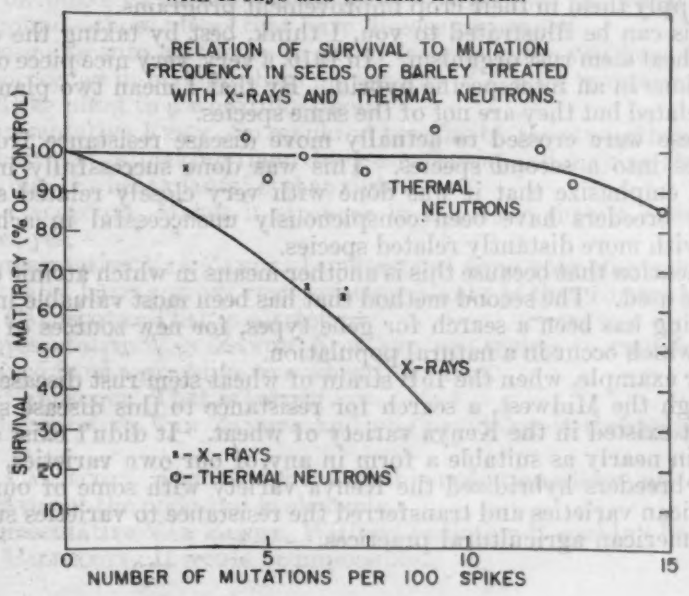
You saw seven pairs on the other slide. Here there are two pairs and all of the other chromosomes have been changed into a large ring. What this means to the plant breeder is that he can go along and he can break off pieces of chromosome, and when he does that, they may rejoin in the manner in which they broke, or another piece of chromosome may join on to that broken end. In this particular case, we have joined up 10. The thing I am trying to illustrate here is, because we will come back to this later, that we can modify the structure of a chromosome with radiation and we can take pieces of chromosome from one region and transplant them to another region by utilizing radiation. This is essentially impossible without radiation.

Representative VAN ZANDT. No doubt, you are talking about one plant when you say from one region to another?

Dr. CALDECOTT. Yes; or a hybrid plant that might occur between two species.

The next slide, please (exhibit 4)?

EXHIBIT 4.—Relation of survival to mutation frequency in seeds of barley treated with X-rays and thermal neutrons.



If one takes thermal neutrons that come from the reactor and one compares the effect of these on dormant seeds with X-rays and compares them on the basis of survival to maturity and the number of the mutations that occur, he finds that with the neutrons he gets a far higher frequency of mutations, that is changes that occur within the chromosome, than he gets with X-rays.

The same thing occurs for the type of chromosomal breaks which I illustrated to you. This is most important to the plant breeder because it tells him he may irradiate a population of material with neutrons and hope to get the beneficial changes as well as the other out of that population with a lot higher frequency when he uses neutrons than when he uses X-rays.

Representative VAN ZANDT. Does he get the benefit of both the X-ray and the thermal neutrons when he uses the thermal neutrons?

Dr. CALDECOTT. Essentially the benefit of both; yes.

Representative PRICE. You have to have a reactor?

Dr. CALDECOTT. One needs a reactor for these studies.

Representative PRICE. An X-ray machine won't do the job?

Dr. CALDECOTT. It will do the job, but much less efficiently. We are far better off to use the neutron source of radiation.

This all means to the plant breeder just precisely what I have told you, that he can induce these changes with the neutron more efficiently than with the X-ray. By irradiating seeds at doses of neutrons or X-rays that will give equal survival, he can expect to induce from 2 to 3 times as many mutants with neutrons as with X-rays.

Needless to say, this piece of basic information is most important because a mutation at best, and particularly one of economic significance, is a rare item. In fact, as a result of these data, the Brookhaven National Laboratory has encouraged the use of neutrons in irradiating seeds and plant material for more than 150 plant breeders.

If one delves into the literature, it is apparent that, for the most part, plant breeders were very quick to grasp basic findings in genetics and apply them in their crop improvement programs.

This can be illustrated to you, I think, best by taking the case of the wheat stem rust organism. In 1916, a very, very nice piece of work was done in an interspecific hybrid. By that I mean two plants that are related but they are not of the same species.

These were crossed to actually move disease resistance from one species into a second species. This was done successfully in 1916, but I emphasize that it was done with very closely related species. Plant breeders have been conspicuously unsuccessful in achieving this with more distantly related species.

I mention that because this is another means in which atomic energy can be used. The second method that has been most valuable in plant breeding has been a search for gene types, for new sources of resistance which occur in a natural population.

For example, when the 15B strain of wheat stem rust disease swept through the Midwest, a search for resistance to this disease showed that it existed in the Kenya variety of wheat. It didn't exist at this time in nearly as suitable a form in any of our own varieties, so the plant breeders hybridized the Kenya variety with some of our local American varieties and transferred the resistance to varieties suitable for American agricultural practices.

Representative VAN ZANDT. How do you spell Kenya?

Dr. CALDECOTT. K-e-n-y-a.

Representative VAN ZANDT. Is that the African Kenya?

Dr. CALDECOTT. The African Kenya. This illustrates the importance of good communication of scientific findings between the various countries.

I think one may rightfully ask two questions. If the genes which naturally exist in our population, which give resistance to disease organisms, are all used up, in other words, we don't have any more naturally occurring genes, do we have any hope of inducing beneficial gene changes?

And secondly, because crosses exist between wide hybrids that result in a grasslike wheat plant that has resistance to certain diseases where the normal wheat plant doesn't, can we hope to take the disease reaction from the grasslike plant and put it into the wheatlike plant and use it for the benefit of mankind?

I think it is a fair statement to say that before radiation we had little hope of doing this, but now we have a great deal of hope of achieving this end. I trust that before this talk is over I can illustrate to you the scope of the opportunities this approach affords.

Representative PRICE. Doctor, to be practical about it, so we can understand you, you say it will benefit mankind. What can you visualize in the evolution of plants for the benefit of mankind?

Dr. CALDECOTT. I will give you an example. Supposing that a virulent race of rust or any other disease organism develops in our agricultural crops—in a wheat plant, for example. Presume that we have no source of resistance to this disease except in related species—in grasses that are related to the wheat plant.

What is the hope of removing this type of resistance from the grass plant and putting it into the wheat plant? The more distantly related these two species are, the less likely is the possibility that we can do it through our conventional methods. With radiation we can break off pieces of chromosome and move them into the wheat plant background—those pieces that have disease resistance.

I am going into this more in detail later to show you how far we have succeeded in making these movements of disease resistance from a grasslike plant to a wheatlike plant.

Representative PRICE. So mankind benefits by the strengthening of the wheat plants, making them disease-resistant, and making stronger plants out of wheat plants; is that right?

Dr. CALDECOTT. Makes it stronger in the sense that it resists the disease; yes.

Representative VAN ZANDT. I understand from your statement that we actually have a grass rust-resisting plant; is that correct?

Dr. CALDECOTT. That is correct.

Representative VAN ZANDT. Now you are trying to transfer this resistance from a grasslike to a wheatlike plant.

Dr. CALDECOTT. That is correct.

Representative VAN ZANDT. And you are doing it through radiation?

Dr. CALDECOTT. That is right; and this radiation allows us to do it and leave out the undesirable elements.

Representative VAN ZANDT. Without radiation it couldn't be done?

Dr. CALDECOTT. It would be impossible.

I want to show you what can be done by changing the individual region and not actually breaking the chromosome. This, then, is the problem of mutation. In the Lee variety of wheat, which is of some economic significance in the Midwest, it turned out that it was susceptible to race 15B and, as you probably know, this race swept through the Midwest and cleaned out a lot of the wheat acreages in 1950 and 1951.

Two scientists, Dr. Hsu and Dr. Ausemus at the University of Minnesota, initiated a program of irradiating the Lee variety to induce resistance to the disease. They have been quite successful. These scientists do not have this new type developed to the point that they can release it to the farmer because they have not conducted yield trials on it, and they haven't done quality studies.

They hope to have a lot of this pertinent information this year and if it turns out that the 15B rust-resistant strain, radiation-induced strain, is better than the Lee for rust resistance and has equal quality and other agronomic characteristics, it can be released to the farmer.

Now, this has not only been done in wheat. It has been done in oats and it has been done in a large variety of oats by scientists at the Brookhaven National Laboratory, the Iowa State College, University of Minnesota, and the University of Florida, and there are enough other scientists working on it so we can expect to see a considerably larger number of examples of this thing before many more years have passed.

Representative VAN ZANDT. When do you apply radiation?

Dr. CALDECOTT. In all of these cases the radiation has been applied to the seed.

Representative VAN ZANDT. What about the production of the plant? How much radiation does it carry?

Dr. CALDECOTT. The plant in these experiments carries no radiation. These scientists are not using isotopes. They are using gamma rays, X-rays, or neutrons. They leave no residual radiation in the plant.

Representative VAN ZANDT. So there is really nothing left in the plant?

Dr. CALDECOTT. No residual radiation or anything of this nature left in the plant.

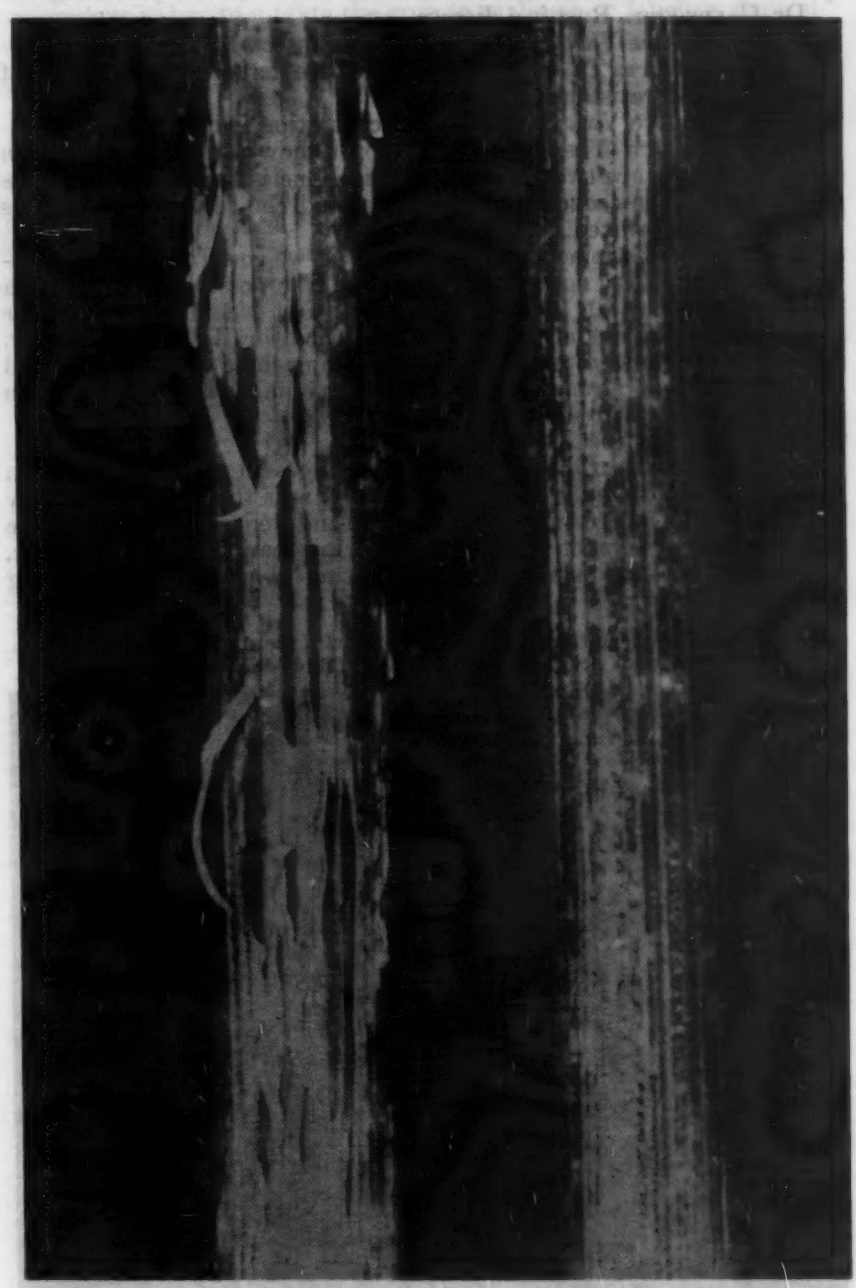
This here (exhibit 5) is an example of a mutation for rust resistance in the Floridaland variety of oats that is utilized a great deal in Florida. This indicates the suceptibility and this is the resistant mutation that came from it. It was produced by Dr. Wallace at the University of Florida.

As with the wheat varieties, these have not been checked to find out whether or not they are equal in other characteristics to the original strain, and I should point out here that one can never be sure that mutation occurs only on one region of the chromosome. It is very likely to carry along other changes which are not beneficial to man, and the plant breeder's job—and this will become more and more apparent as time goes on—is to remove the good things after radiation through his conventional breeding programs and get rid of the bad things. This has proven relatively easy to do in some of the studies that have been conducted, but virtually impossible in others.

I will illustrate that to you in a moment. The next slide, please.

I wanted to show you just what I mean by some of the harmful things. This happens to be a dwarf plant in the normal variety of oats which has rust resistance. The object now would be to get rid

EXHIBIT 5.—Thermal neutron induced rust resistance in the Floridaland variety of oats. Courtesy of A. Wallace, University of Florida, Gainesville.



of the dwarfness and maintain the good. This could probably be done by crossing this plant and crossing that plant, backcrossing, always selecting for the disease resistance when it occurred free from the dwarf habit.

Representative VAN ZANDT. You said so far we are able to produce a plant to resist disease as well as rust.

Dr. CALDECOTT. Rust is a disease.

Representative VAN ZANDT. How about insects?

Dr. CALDECOTT. To my knowledge, there have been no cases of insect-induced resistance.

Representative VAN ZANDT. So concentration is on disease?

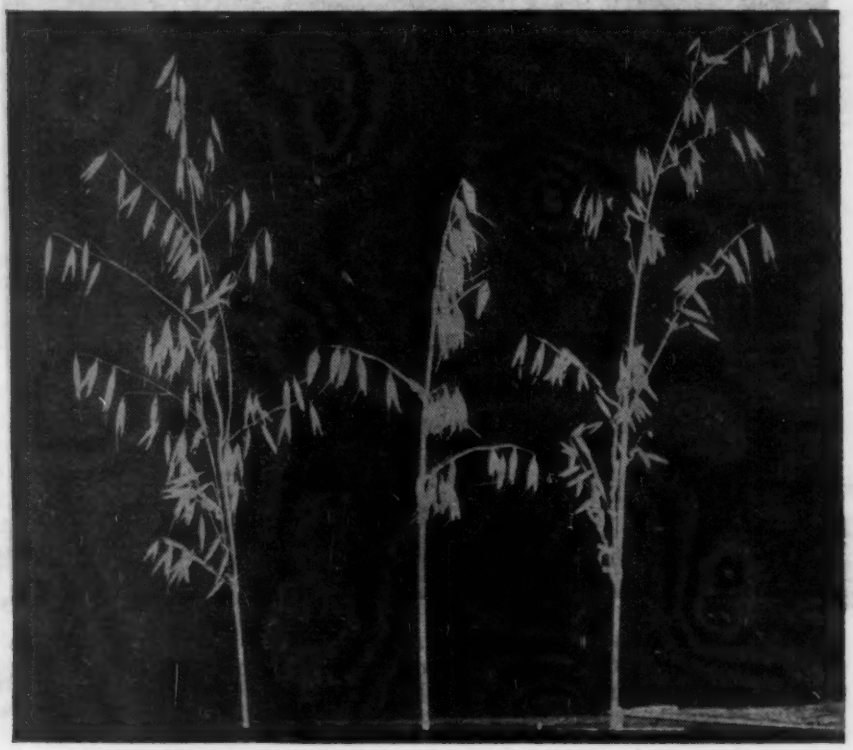
Dr. CALDECOTT. Yes, for the most part they are concentrating on disease. There are two reasons for this: One is that the disease has such tremendous economic significance, and the second is that it is very easily recognized.

It would be of tremendous value to us if we could go into a grass-like plant, and here again I think it would be possible. Let's take a winter hardy wheat plant, grass plant, and we move the winter hardiness and transfer it into some agriculturally useful variety. This we have some hope of doing by breaking these chromosomes and moving pieces of chromosome over. We have made small advances in this regard at the present time.

The next slide, please.

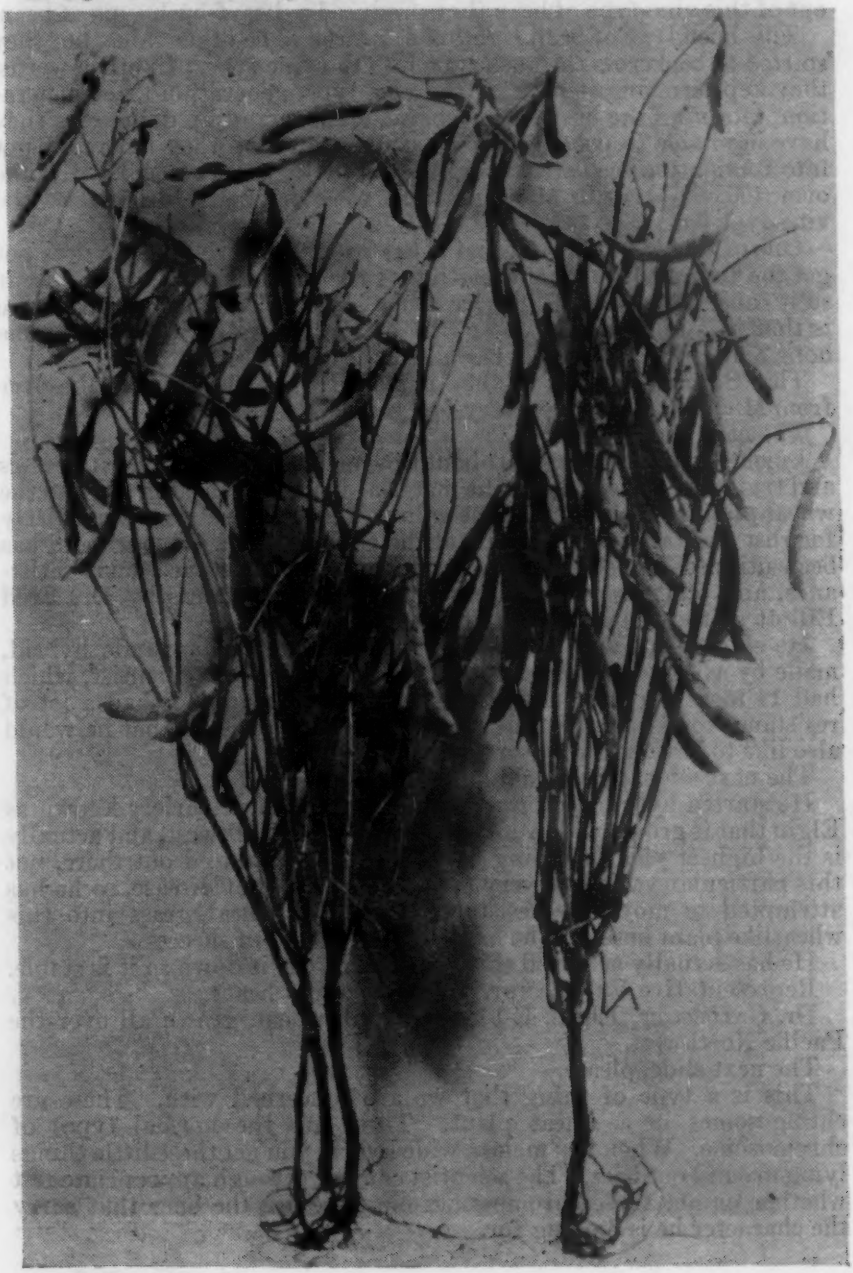
This is an indication of the various ranges in maturity that can come from irradiated seed (exhibit 6). This is the standard variety of oats and these are two of the neutron-induced mutants that came out of it. They happen to be later maturing than the Huron variety, but we also can induce changes that bring about earlier maturing types.

EXHIBIT 6.—Maturity difference in oats induced with thermal neutron irradiation. Courtesy of A. Wallace, University of Florida, Gainesville.



Obviously, where there is a short growing season and where one is trying to escape disease through a short growing season it could be of tremendous value, to mutate the crop to earliness or lateness, depending on the type of climate in which we wish to grow it.

EXHIBIT 7.—Sanilac bush bean developed from the vine-type Michelite after treatment with X-rays. (See text.) Courtesy of E. E. Down and A. L. Andersen, Michigan State University.



82499°—56——2

The next slide, please.

I think probably the best example of what has been done with radiation in agricultural crops to literally produce a crop that is more valuable to mankind, the best example I can give you, is this case of the Michelite bean (exhibit 7) that is characteristically a vine or a navy-type bean. Drs. Down and Andersen at Michigan State University irradiated some of these bean seeds in 1941 with X-rays and out of this vine-type of bean they produced a dwarf-bush type of bean.

This bush type of bean right off appeared to be of no value, but they started to backcross the bush type into the vine type. In other words, they kept crossing it back on the vine type, generation after generation, retaining the bushy-type characteristics, and by doing this they have been able to produce these bush beans which they have now got into foundation seed stocks and they actually expect that it will take over 400,000 acres in Michigan that were originally devoted to the vine-type bean.

One of the advantages is that it has an open crown and one does not get the fungus diseases and rotting of the plant that commonly occur so it can take a good deal more wet weather. The second advantage is that it is upright. It doesn't lie on the ground. So there is some hope a mechanical harvester can be used to harvest it.

This Sanilac variety, as they named it, they think will take over from Michelite in the next very few years.

The next slide, please.

I mentioned earlier to you about this business of using wheat grasses and trying to move some of the material from the wheat grass into the wheat plant so it will be of some value. This has been done very nicely for rust resistance by Dr. Sears at the University of Missouri, and has been utilized a good deal for producing rust resistance, bunt resistance, and other types of disease in wheat type plants by Dr. Fred Elliott at the State College of Washington.

He started out with a hybrid which is known as a Sando hybrid, made by a United States Department of Agriculture scientist, which had 14 more chromosomes than the wheat plant, but it had a lot of resistance to disease. It had some other characteristics that he would also like to have in the wheat plant.

The next slide, please (exhibit 8).

He started hybridizing that with this club wheat variety known as Elgin that is grown widely all over the Pacific Northwest, and actually is the highest yielding thing they have ever produced out there, but this particular variety is very susceptible to a bunt disease, so he has attempted to move the resistance from this wheat grass into this wheatlike plant here, and he has had a great deal of success.

He has actually achieved this goal and he has it down so it is stable.

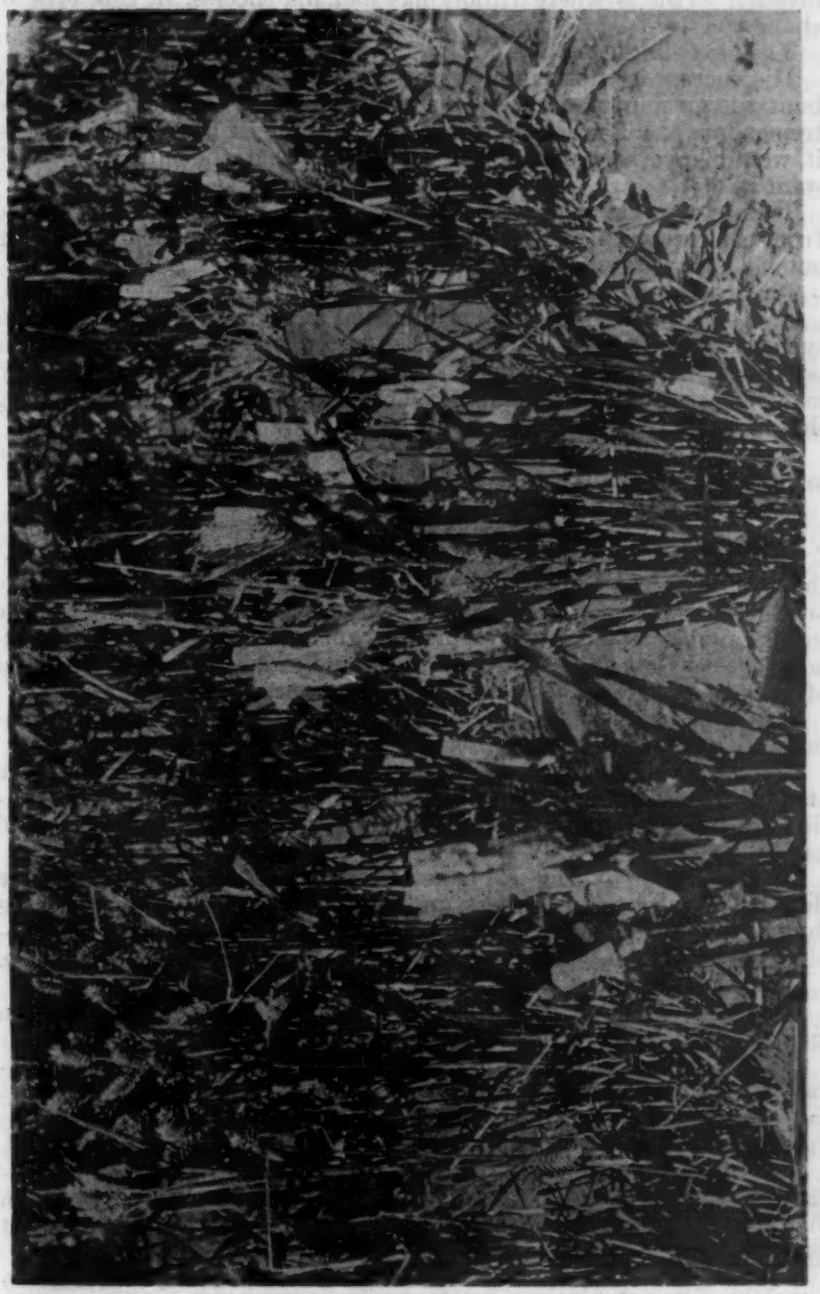
Representative VAN ZANDT. What type of wheat?

Dr. CALDECOTT. Elgin, E-l-g-i-n, a club wheat, grown all over the Pacific Northwest.

The next slide, please.

This is a type of thing that we are concerned with. These are chromosomes in a wheat plant. These are the normal types of chromosome. When you make a wide hybrid you get these little things lying around out here. The scientist can tell through appropriate test whether or not these chromosomes out here are the ones that carry the character he is looking for.

EXHIBIT 8.—Bunt resistant Elgin-type club wheat from a cross involving *Triticum Vulgare* and *Agropyron elongatum*. Derived line in foreground resulted from thermal neutron irradiation of Hybrid Elgin × (*T Vulgare* × *A. elongatum*) backcrossed to variety Elgin. (Courtesy F. C. Elliott, State College of Washington.)



When they do, he bombards these with radiation and he attempts to move a piece of this chromosome into these normal types. That is precisely what he is trying to do with radiation and this is, I think, one of the really important ways radiation can be of value to the plant breeder. This is where Elliott has had his success, in this type of change.

The next slide, please.

His success is illustrated by this particular slide here. This is a bunt susceptible plant. The yield of this plant would be reduced tremendously. The wheat would probably be of little value because it would have so much of the smut in it that the miller wouldn't want it.

This is a strain which he is backcrossing, which he has obtained from this program, that he hopes he can use agronomically and put out at a later date as a variety.

The next slide, please.

This slide I am using to illustrate what he is doing. This resistance type here is backcrossed onto this susceptible type, but desirable because of its yield and other characteristics. He does this for many, many generations and ultimately hopes to come out with something that is useful to mankind.

Representative VAN ZANDT. Doctor, does he do anything to the moisture in the plant?

Dr. CALDECOTT. To make it withstand drought?

Representative VAN ZANDT. Yes.

Dr. CALDECOTT. These are the types of things that I mentioned that would be much more difficult to pick up than disease resistance but there is no reason that I can see why a scientist should not be able to take plants which are drought tolerant and hybridize them on related species that we use agronomically and attempt to move this kind of character over into the agriculturally desirable plant.

It is a lot tougher to do because it is relatively easy to spead a disease. It is pretty rough to spread a drought, as you perhaps know.

I think I can sum this all up, gentlemen, by saying that we have at this time a lot of indications that we can do many things with radiation to improve our agricultural species, many things of a genetic nature.

We need a lot of time to make these changes, to test them before they can be released to farmers, and perhaps the most important thing that the plant breeder needs is a good deal of confidence from the people with whom he works and the people to whom he is responsible.

Thank you.

Representative PRICE. Doctor, have any of these tested plants been introduced to farmers, or are they still in laboratories?

Dr. CALDECOTT. This Sanilac variety has been reduced to the foundation seed grower. He is more or less the elite farmer and that variety unquestionably will be released. All of the other varieties are in the stage of testing and naturally these tests have to be very critical.

One can't take a chance on releasing something that would perhaps have poorer quality or lower yield. He must make really certain that he has something that is at least the equivalent of those that already exist.

Representative VAN ZANDT. Would you care to make a prediction as to when the disease-resistant bean seed will be made available to the farmers of the country?

Dr. CALDECOTT. The bean variety again—I come back to that because it is the nicest—will undoubtedly be released next year. Some of the wheat varieties need more checking, as do some of the oat varieties.

Representative VAN ZANDT. Would you say, within 2 or 3 years?

Dr. CALDECOTT. I would qualify it and say that if they have the quality and the yield and they are not carrying these other harmful characteristics that I mentioned, these will be released in 2 or 3 years.

If they are carrying these characteristics, the plant breeder will have to work with them to place the disease resistance in a better genetic background.

Representative VAN ZANDT. Could you make a prediction as to the savings to the farmers of this country when the disease-resistant plant has been perfected?

Dr. CALDECOTT. I am a poor economist, but if one has ever walked through a field that is smitten with rust and seen the way the yield can be reduced from perhaps a potential of 30 bushels to 5 or 6, and then of poor quality wheat, there is just no question this would turn out in terms of millions of dollars. As for figures, I couldn't give them.

Representative VAN ZANDT. Doctor, are you satisfied with the effort that is being made in this field by the AEC?

Dr. CALDECOTT. I think the Atomic Energy Commission has done an excellent job of stimulating this type of research. In fact, through their laboratory at Brookhaven they have actually shown the way.

The universities have been quick to grasp on to it and the United States Department of Agriculture is making large efforts in this connection.

Representative VAN ZANDT. How many separate and distinct projects are involved?

Dr. CALDECOTT. Perhaps Dr. Dunham would answer that.

Representative VAN ZANDT. I am speaking of the number of universities that are involved.

Dr. DUNHAM. On just the plant breeding?

Representative VAN ZANDT. Yes.

Dr. DUNHAM. I am afraid I would have to look that up, but I would be glad to provide the committee with it.

Representative VAN ZANDT. Is it possible to give us your estimate?

Dr. DUNHAM. If I could run through this for a second, I can give you a rough figure. I don't think I could get it from this, for one reason that there are certainly 6 or 8. This is a list of the offsite work that we support at universities and so forth. A great deal of the work which Dr. Caldecott has spoken about is a cooperative thing where they will get the irradiations done at the Brookhaven Laboratory, or now at the University of Tennessee agricultural project, and then the scientists from the home laboratory take them back, and with their own funds and facilities go ahead and do the studies, and I have no way of knowing how many of those are going on now, but it is a great number.

Representative PRICE. Dr. Caldecott, do you operate under contract with the AEC?

Dr. CALDECOTT. Yes; I am actually employed by the United States Department of Agriculture, and I have a contract with the AEC that is worked out jointly between the University of Minnesota, the United

States Department of Agriculture, and the Atomic Energy Commission.

This is an exceedingly happy relationship. We can do our research in a way that would be impossible if any one of us had to rely solely on our own facilities.

Representative VAN ZANDT. Doctor, in addition to disease resistance, can you see any other benefits that irradiation will produce in plant life?

Dr. CALDECOTT. I can only mention again that I am of the opinion there is every reason to believe that we can introduce pieces of chromosome from distantly related species that may have, for example, drought resistance, or a solid stem that could resist the saw fly into our wheats.

These are all things on which a great deal of research needs to be done and they are things that will not pay off for perhaps 15 or 20 years. We have to get a backlog of basic information and find out what is possible, how far can we go toward moving these things over, and this information we don't have.

Representative VAN ZANDT. Dr. Dunham, how much money are we spending in this particular field today from the AEC standpoint?

Dr. DUNHAM. Just on this irradiation?

Representative VAN ZANDT. Yes. Is it possible to break the amount down and give us a figure?

Dr. DUNHAM. I couldn't give you a figure offhand, I am sorry to say, because of the fact that so much of the irradiations are done at AEC laboratories and to try to estimate what that costs would be the wildest sort of guess.

Representative VAN ZANT. Did I understand you to say that these contractors also are spending some of their money?

Dr. DUNHAM. Yes. The universities and the agricultural experiment stations are all putting effort into it.

Representative VAN ZANDT. Then it is really a joint effort?

Dr. DUNHAM. It is a joint effort across the country.

Representative VAN ZANDT. Between the Federal Government and various universities?

Dr. DUNHAM. Yes; both private and State universities.

Representative PRICE. Thank you very much, Dr. Caldecott, for your very interesting and enlightening presentation. I want to compliment you and your organization on the work that you are doing.

Dr. CALDECOTT. Thank you, sir.

Representative PRICE. Dr. Dunham, will you present your next witness?

Dr. DUNHAM. The next scientist to present material before the committee is Dr. Thorne, director of the Utah Agricultural Experiment Station, Utah State Agricultural College, at Logan, Utah.

He will talk about how radioisotopes help solve plant nutrient problems of desert areas. Dr. Thorne?

STATEMENT OF DR. DAVID W. THORNE, DEPARTMENT OF AGRONOMY, UTAH STATE AGRICULTURAL COLLEGE, LOGAN, UTAH

Dr. THORNE. Mr. Chairman and Mr. Van Zandt, we have had great help in our arid regions from the use of radioisotopes. I am a soil scientist myself, and have been interested in soils and plant nutrition. I would like to illustrate the area which I am interested in.

This map (exhibit 9) represents the arid part of the United States, where we have generally about 20 inches or less of rainfall per year, and we have many peculiar problems in this area which to people who live in the more humid parts of the country are rather foreign to their way of thinking, and to their type of agriculture.

The peculiar thing which I am concerned about today is that in this area lime tends to accumulate in soils so that the soils, as time goes on, tend to be more alkaline, whereas in this part of the area, which has

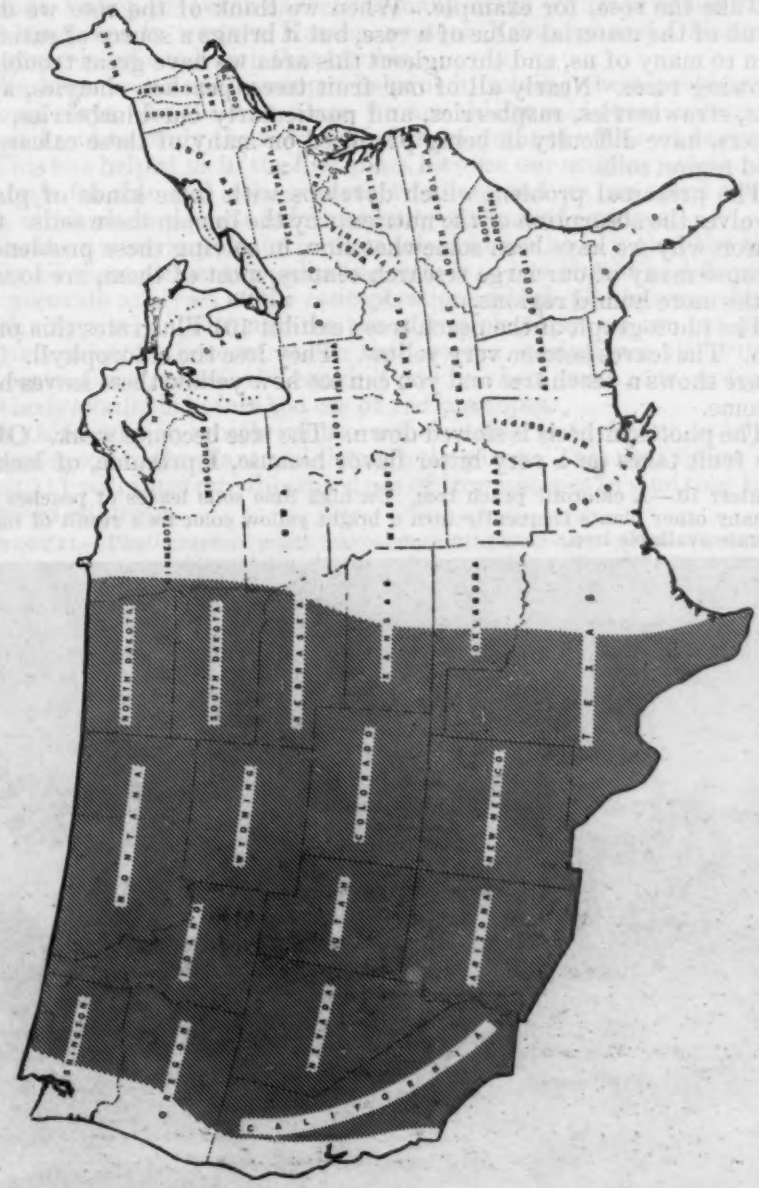


EXHIBIT 9.—The shaded portion indicates the arid region of the United States where lime tends to accumulate in soils.

perhaps more intensive agriculture, the higher rainfall leaches the lime out of the soils and they become more acid, so we are continually having to add lime.

This problem of the lime accumulating in the soil has introduced many peculiar problems, and this results largely from certain of our plants being sensitive to lime. These plants that are sensitive to this lime in the soil include many of the plants that we are greatly concerned with and which we prize highly, including many of our ornamentals.

Take the rose, for example. When we think of the rose we don't think of the material value of a rose, but it brings a source of satisfaction to many of us, and throughout this area we have great trouble in growing roses. Nearly all of our fruit trees, peaches, cherries, apricots, strawberries, raspberries, and particularly our blueberries, and others, have difficulty in being produced on many of these calcareous arid region soils.

The principal problem which develops with these kinds of plants involves the absorption of the nutrients by the lime in these soils. One reason why we have been somewhat slow in solving these problems is because many of our large research centers, most of them, are located in the more humid regions.

The photograph of the peach tree (exhibit 10) illustrates this problem. The leaves become very yellow. They lose the chlorophyll. The figure shows a peach tree and you can see how yellow these leaves have become.

The photosynthesis is slowed down. The tree becomes weak. Often the fruit takes on a very bitter flavor because, I presume, of lack of

EXHIBIT 10.—A chlorotic peach tree. On high lime soils leaves of peaches and many other plants frequently turn a bright yellow color as a result of inadequate available iron.

certain sugars being produced in the leaves. The trees become weaker and die when we get a hard winter.

Some areas of our fruit-producing areas of the West go out of fruit production because of this accumulation of lime. Often lime accumulates from irrigation waters and tends to become worse as time goes on. Some of our irrigation waters contain bicarbonate, which accentuates the problem. Many of our fruit areas, like Yakima and Wenatchee in Washington, the central area of Utah, the central valley of Arizona, much of the area in southern California, the Rio Grande Valley in Texas as well as many areas which produce beans and sorghums in western Kansas, western Nebraska and Oklahoma, are severely affected with this trouble.

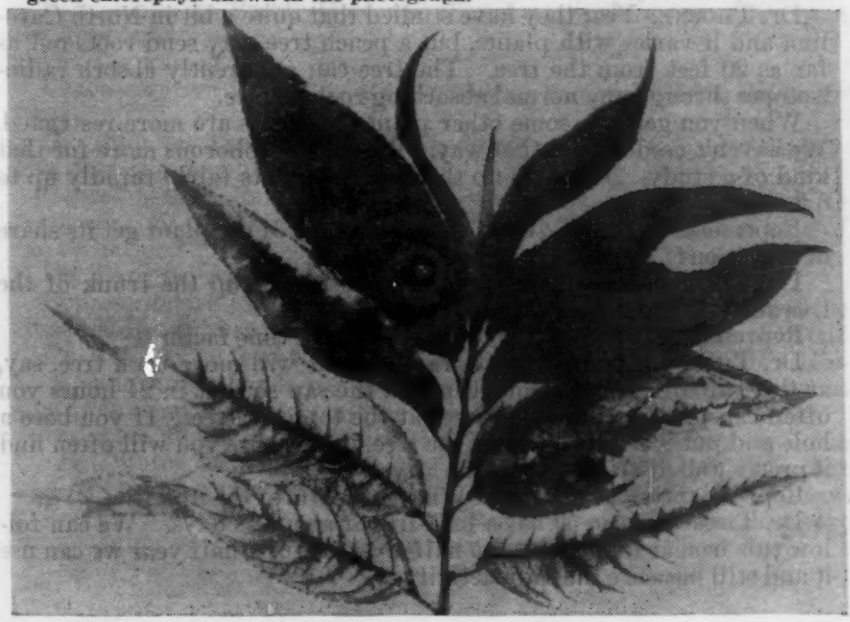
We have found radioisotopes helpful in solving these problems in several ways. In the first place, we are able to add these isotopes to the soil and to study the reactions of these isotopes with soil particles.

This has helped us in the first place because our ordinary method of analysis for zinc and iron, are rather tedious and we can speed up the rate at which we can get information by the use of isotopes.

Perhaps more important in the analytical methods is that the solubility of these elements in alkaline soils is so low that it is difficult to get accurate analyses at the concentrations which plants seem able to work effectively. Through the use of radioisotopes we can get down to such sensitive concentrations that we can study these elements in concentrations where we couldn't study them with our ordinary methods available before the use of radioisotopes.

A third way in which we use radioisotopes is to follow nutrients from the soil to the plant and through the plant. This next figure (exhibit 11) will illustrate this third use of iron isotopes in studying lime-induced chlorosis.

EXHIBIT 11.—Photograph of peach leaves containing radioactive iron. When these leaves were pressed against a photographic plate the radioactive iron exposed the film and showed the iron to be located in the same leaf area as the dark green chlorophyll shown in the photograph.



On the left we have peach leaves wherein we have photographed the leaves as they were taken from the tree. The lower leaves are chlorotic with just a little green showing along the veins. The upper leaves are normal with the chlorophyll being fairly general throughout. The tree on which these leaves were produced was fed radioactive iron. On the right we see a radioautogram of the same leaves shown on the left. The leaves were pressed against a photographic plate and the location of the radioactive iron was recorded on the film. In the green leaf, you see, the iron is very uniformly distributed. In the chlorotic leaves the iron has been precipitated along the veins.

We have trouble, in other words, with the iron moving about the leaf and getting into the position where it can help to form chlorophyll and make use of the sunlight. The iron, even though it gets into the plant, may be precipitated.

Representative VAN ZANDT. Doctor, how do you apply your application of the isotope?

Dr. THORNE. We apply it in several ways. Most of these studies, because of the difficulty of using isotopes in the field, are handled in the greenhouse and we put the iron in the medium around the roots or inject it into the plants. We obtain the isotope from Oak Ridge. It comes in a solution and we mix that up with some inactive iron to the level of activity we want it. We can either add it to the soil or to a solution and it enters the plant through the roots and goes up through the plant.

Representative VAN ZANDT. To what area around the plant do you apply it?

Dr. THORNE. We put it right close in. We may bore a hole in the trunk of the plant and put it right in the trunk or we put it in a solution where the roots are growing. Usually these experimental plants are growing in a small pot or container of a gallon or two in size.

Representative VAN ZANDT. Does your experience reveal how far out the plant could reach to absorb this radiation?

Dr. THORNE. Yes; they have studied that quite a bit in North Carolina and it varies with plants, but a peach tree may send roots out as far as 20 feet from the tree. The tree can apparently absorb radioisotopes through any normal absorbing root surface.

When you get into some other plants the roots are more restricted. We haven't used iron in that way. We use phosphorous more for that kind of a study. It moves up through the plants fairly rapidly up to 3 feet an hour.

Representative VAN ZANDT. Does the stock of the plant get its share of radiation?

Dr. THORNE. Yes; it tends to accumulate all up the trunk of the tree and be precipitated all the way along.

Representative VAN ZANDT. How about the time factor?

Dr. THORNE. It moves quite rapidly. It will move up a tree, say, at the rate of 2 feet an hour through the sap so that in 24 hours you often can pick it up in the leaves at the top of a tree. If you bore a hole and put it in the trunk of the tree, in 24 hours you will often find it pretty well distributed into the leaves.

Representative VAN ZANDT. What is the life of the iron?

Dr. THORNE. Iron 59 has a half-life of about 48 days. We can follow this iron at least for 4 or 5 half-lives, so for a half year we can use it and still measure the radioactivity.

Representative VAN ZANDT. This isotope, as I understand it, is being used to improve the fertility of the soil which, in turn, helps the plant or the tree; is that right?

Dr. THORNE. Yes.

Representative VAN ZANDT. Does the irradiation of the plant or the tree resist disease?

Dr. THORNE. No; we are not using it in that way, to help resist disease. We are using this merely as a way to study these problems. Of course, as Dr. Caldecott pointed out, they can change the inheriance of a plant and get disease resistance into it, but that is not the purpose of these studies. It is merely to use this as a tool to learn about problems of importance to the farmer.

Representative VAN ZANDT. Has it had any effect today on the products of the plant or the tree?

Dr. THORNE. You mean the influence of this on yields?

Representative VAN ZANDT. Yes.

Dr. THORNE. We have not been using this in that manner, to study the influence on yields. The United States Department of Agriculture, in cooperation with the State experiment stations, studied this. They found essentially no effects of radiation on yields.

Representative VAN ZANDT. Is there any poison left in the plant or tree?

Dr. THORNE. Well, the radiation, of course, is dangerous to all kinds of life and when we are through with our experiment we destroy the trees and put them in a pit where they won't cause any damage to life, but the radioactivity gradually disappears.

Representative PRICE. Are you optimistic about your research?

Dr. THORNE. Yes; we feel we have made great progress in this particular line of work. One of the things that we are particularly concerned about is why does this lime cause this problem, and even though there are literally thousands of papers published on this subject, not much progress was made until the use of radioactive elements.

Representative PRICE. However, they were working on research on the problem?

Dr. THORNE. Yes.

Representative PRICE. And got nowhere, evidently, with the problem?

Dr. THORNE. That is right. They knew something about the problem, that iron would help control it.

Representative PRICE. How many years would you say they have been working on the problem before radiation, excluding the idea of the radiation?

Dr. THORNE. About 30 or 40 years at least.

Representative PRICE. What would you say is the comparison of the research during that period and research in your period of irradiation?

Dr. THORNE. All of this progress has not been the result of radiation, understand, but in the last 10 years we have learned more about this by far that we knew in all the time before.

We have found in Utah and at the salinity laboratory, and the United States Department of Agriculture at Riverside, Calif., that one of the important causes of this trouble is the bicarbonate ion. When you add water to a soil containing lime, some lime breaks apart into calcium ions and bicarbonate ions, principally.

The bicarbonate ions seem to have a distinctive effect upon these plants that are sensitive to lime chlorosis, and it causes the iron to precipitate in the plant. We don't know just why yet, but it does reduce the mobility of the iron, and it also tends to inactivate certain of the enzyme systems, in which the iron is the important functional part, or one of the important functioning parts.

I believe there is a slide or two that illustrates the bicarbonate problem. Some earlier work had indicated that the bicarbonate ion was not taken up by plants. Apparently, however, some plants can absorb appreciably carbon from bicarbonate ions in calcareous soils.

The fourth figure (exhibit 12) shows a bean plant grown in a solution containing a small amount of bicarbonate ion made in part with

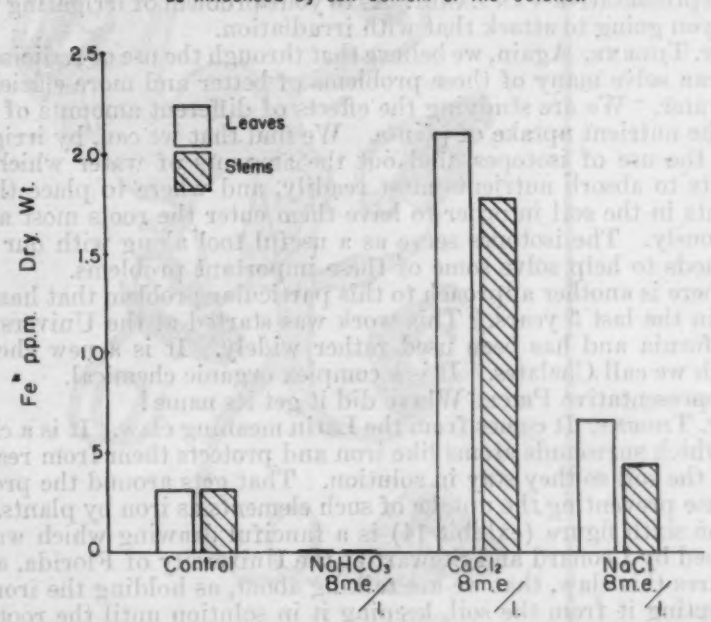
EXHIBIT 12.—Radioautogram of bean leaves showing a general distribution of radioactive carbon absorbed from a bicarbonate solution around the plant roots.

radioactive carbon. One of these plants was pressed against a photographic film. The figure shows the location of the radioactive carbon taken from the bicarbonate around the roots. This radioautograph shows that plants can absorb appreciable amounts of bicarbonate ions through the roots.

This bicarbonate ion, when it gets inside, before it changes over to sugars or other compounds, seems to have an effect in inactivating some of the enzyme systems.

The fifth figure (exhibit 13) shows the effect of bicarbonate on iron absorption by bean plants. The plants growing in the bicarbonate-containing solution became chlorotic and did not absorb the radioactive iron. Plants growing in the solution containing calcium chloride absorbed iron even fasten than the control.

EXHIBIT 13.—Graphs showing that radioactive iron content of bean leaves is reduced by sodium bicarbonate in a solution culture.



The radioactive iron enables us to separate the iron absorbed here during a short period from the iron that had been taken in before.

The bicarbonate and the calcium are principal ingredients of calcareous soils. Iron was absorbed in the presence of sodium at somewhat the same rate as in the control cultures, so it seems that the calcium was helping to perhaps even increase the absorption of the iron, and the bicarbonate was reducing absorption. This has helped us to pinpoint this effect of bicarbonate in tying up iron.

Representative VAN ZANDT. Doctor, looking at the arid area there and taking into consideration your accomplishments to date, as you project your thinking far into the future, what can you see for that part of the United States

Dr. THORNE. We have tremendous production potentials in this irrigated area with a lot of sunshine and long growing season for much of it. Water is the limiting factor. We don't know what effect cloud seeding and some of these things may have as yet. They haven't contributed much in a practical way as far as we can tell, but we believe if we can change the enzyme systems of plants and substitute certain other types of enzymes for these that are sensitive to bicarbonate, it would seem quite feasible that we can get rid of the chlorosis problem and lower our production costs of many plants.

In addition we get away from many of the problems you have in the East. We don't have to add lime to the soil. We don't have the problem of acidity.

Representative VAN ZANDT. As I see it, through the application of radiation, you are going to attack the lime problem.

Dr. THORNE. We are going to try and find ways to get around the problem. We will not get rid of the lime. Some of these soils contain as high as 1,000 tons of lime per acre in the upper foot of soil.

Representative VAN ZANDT. As to your problem of irrigating water, are you going to attack that with irradiation.

Dr. THORNE. Again, we believe that through the use of radioisotopes we can solve many of these problems of better and more efficient use of water. We are studying the effects of different amounts of water on the nutrient uptake of plants. We find that we can, by irrigation and the use of isotopes, find out the amounts of water which help plants to absorb nutrients most readily, and where to place the nutrients in the soil in order to have them enter the roots most advantageously. The isotopes serve as a useful tool along with our other methods to help solve some of these important problems.

There is another approach to this particular problem that has come out in the last 5 years. This work was started at the University of California and has been used rather widely. It is a new chemical which we call Chelates. It is a complex organic chemical.

Representative PRICE. Where did it get its name?

Dr. THORNE. It comes from the Latin meaning claw. It is a chemical which surrounds atoms like iron and protects them from reacting with the soil so they stay in solution. That gets around the problem of lime preventing the uptake of such elements as iron by plants.

The sixth figure (exhibit 14) is a fanciful drawing which was developed by Leonard and Stewart at the University of Florida, and it pictures this claw, that we are talking about, as holding the iron and protecting it from the soil, keeping it in solution until the roots can surround and absorb it.

Dr. Jacobsen, at the University of California, first found that chelates would help plants absorb iron from solutions. It was later used to treat iron-deficient soils in Florida. This same chelate would not work in the alkaline soils of the West. Later, other types of chelates have been produced that enable plants to take up iron from our western calcareous soils.

We can put a pound or more of chelate containing iron around a chlorotic tree and it will cause the tree to turn a bright green and stay quite normal for some time, whereas if we were to take this iron in the ordinary forms we have been using, we can put many pounds around a tree and it won't be effective because it precipitates rapidly and has only a very temporary influence on the plant.

EXHIBIT 14.—Chart showing concept of chelate action. (Redrawn from a diagram illustrating What Chelates Are, by I. Stewart and C. D. Leonard in the National Fertilizer Review, October, November, and December 1954.)

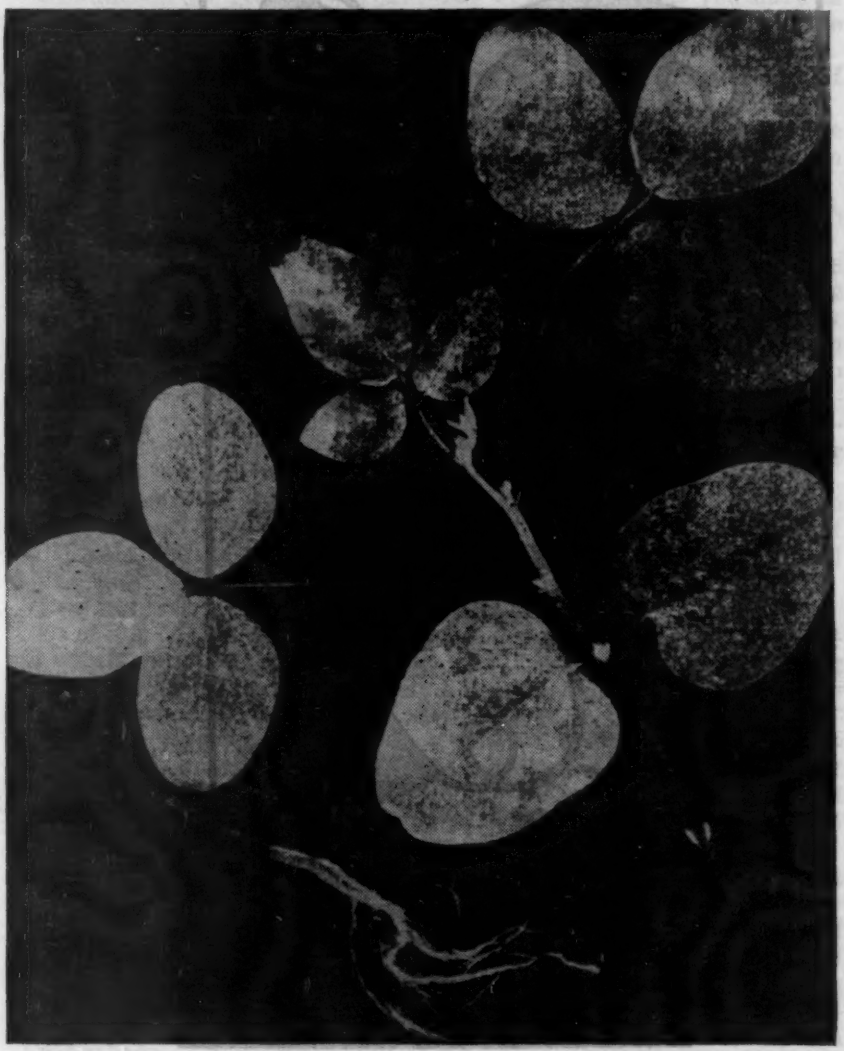
CHELATES
Fe
Plant roots taking up chelate and iron. In the artist's conception the chelates (claws) grasp and surround the iron in the soil. The entire mass is absorbed by the plant roots. Somewhere within the plant the iron is separated from the chelate.

We have been wondering how these chelates work, so they have put some radioactive carbon into the chelate and used it for plant studies. Dr. A. Wallace, at the University of California at Los Angeles, has been working with this for some time. Dr. J. C. Brown, here at

Beltsville, also has been working with it. They find it gets in. Then this radioactive carbon seems to separate from the iron and apparently there is a breakdown of the chelate within the plant.

The seventh figure (exhibit 15) shows a radioautogram of leaves receiving chelated radioactive iron. Now we note in contract to previous figures that the iron is evenly distributed throughout the leaves where it can be effective.

EXHIBIT 15.—Radioautogram of soybean plant containing radioactive iron fed in chelate form, showing uniform distribution throughout the plant. (Reproduced from R. S. Holmes and J. C. Brown, Soil Science 80: 167–179, 1955.)



Representative VAN ZANDT. Does this stunt the growth of the plant in any way?

Dr. THORNE. No; not at the levels we use it. You have to get rather high amounts of radioactive materials in plants and it only takes a small amount of iron, or zinc, or some of these elements to

make a plan grow quite normally if it is in the right form. At the levels we use it there is no measurable bad effect on the plants.

Representative VAN ZANDT. What about the nonarid sections of the United States and what are you doing there? Do you have a program to improve the fertility of the soil in any way?

Dr. THORNE. Yes. You must understand I am from Utah and my main concern is getting these arid countries to produce rather than worrying about the East. But many studies are being reported involving the use of radioisotopes from every part of the United States.

I mentioned the work in Florida and Beltsville. Radioactive phosphorus is being used in nearly every State. Other radioisotopes are being used where there are special problems, such as zinc and sulfur deficiencies.

Representative VAN ZANDT. Doctor, I take it from your statement the isotope will be beneficial by increasing the fertility of the soil all over the Nation.

Dr. THORNE. Isotopes are giving us the basic information which we need to understand soils and plant nutrition problems and interrelationships between the two all over the country; yes.

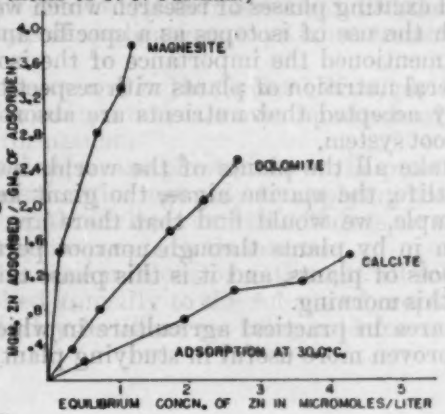
Representative VAN ZANDT. Has your program taken you abroad to any other section of the world?

Dr. THORNE. No; it has not. We have large numbers of men come to our college, as others have, from abroad, but I myself have not been abroad.

In the West we also have a problem with zinc and radioisotopes have been used in studying it in much the same way as with the iron problem. Fruit trees and in some areas general field crops are affected. In fruit trees zinc deficiency is know as little leaf and as dieback.

The use of radioisotopes has enabled us not only to follow zinc through the plant, but to pinpoint just where it is absorbed in the soil. We have the problem of zinc being absorbed on lime. We have been studying the chemistry of this and with just the pure calcium lime zinc is absorbed at a minimum. As the proportion of magnesium in lime is increased zinc is much more strongly absorbed. The difference in absorption on three types of lime particles is shown in exhibit 16.

EXHIBIT 16.—Graph showing the different energies of zinc absorption on three forms of lime. Zinc is absorbed more strongly as the proportion of magnesium increases. (From thesis of J. J. Jurinak.)



82499°—56——3

Zinc is absorbed on lime particles at the sites occupied by magnesium atoms in the lime particles. Now we understand the problem of zinc more clearly than before, and we are able to follow it through soils and plants much the same as we have with iron.

In Columbia in Tennessee they have a very extensive zinc problem, and it is again absorbed apparently on some of these magnesium phosphate particles, and corn is badly affected in addition to the fruit crops in that area. We have used it in fertilizer and phosphate fertilizers have been tried throughout the country, and we have been able to evaluate them by measuring how fast the various phosphates move from the fertilizer to the plant.

I think I should not spend more time on this, but it has given us a new insight into the nutrition of plants and how to produce crops more effectively and use our land more wisely.

Representative VAN ZANDT. Have you carried on a program in the grazing areas?

Dr. THORNE. We have not used radioisotopes in our grazing areas to any extent, but we have used them with range plants which we bring into the greenhouse and use, where we study them under controlled conditions, and study their nutrition there.

Representative PRICE. Does that conclude your statement?

Dr. THORNE. I think that concludes my statement.

Representative PRICE. Thank you very much, Dr. Thorne, for a very interesting and important project.

Dr. Dunham?

Dr. DUNHAM. The next scientist who has prepared a report for the subcommittee is Dr. S. H. Wittwer, professor of horticulture, Michigan State University, College of Agriculture, East Lansing, Mich. He will discuss radioactive isotopes in studies of foliar feeding of plants.

Representative PRICE. Dr. Wittwer?

STATEMENT OF DR. SYLVAN H. WITTWER, DEPARTMENT OF HORTICULTURE, MICHIGAN STATE COLLEGE, EAST LANSING, MICH.

Dr. WITTWER. Mr. Chairman and members of the committee and those who are here assembled, it is a privilege to come from the State of Michigan to discuss with you and to inform you of one of the most interesting and exciting phases of research which we feel is now being conducted with the use of isotopes as a specific and accurate tool.

Dr. Thorne mentioned the importance of the isotope technique in studies of mineral nutrition of plants with respect to root absorption. It is commonly accepted that nutrients are absorbed by plants primarily by the root system.

Yet, if we take all the plants of the world, including the lower forms of plantlife, the marine algae, the giant kelps, and Spanish moss, for example, we would find that there are as many mineral nutrients taken in by plants through nonroot portions as there are through the roots of plants, and it is this phase that I would like to deal with here this morning.

There is no area in practical agriculture in which the radioactive isotopes have proven more useful in studying plant processes than in

tracing the absorption and transport of nutrients applied as sprays. The concept that leaves and other aerial plant parts may function as nutrient absorbing organs of sufficient importance to markedly alter the nutritional status of a plant is contrary to what is written in many textbooks, is still held in reservation by some plant physiologists, and remains somewhat unpopular with many agronomists and soil scientists. There are many biologists who yet feel that the leaves of plants are covered with an impermeable cuticle which will not permit the penetration of mineral nutrients that are sprayed on the leaves of plants, and yet this principle of leaf absorption, the uptake of nutrients by parts of the plants which are not roots, has been recognized, and it has been accepted and put into practical production for several decades.

I would like to refer to one of the early reports, about 66 years ago, published in the American Agriculturist, May 1890. The subject has to do with liquid manuring in Germany, and I will quote directly from that old publication on the subject which we are dealing with this morning. It states:

> In this part of the world the manure is applied to the garden in liquid form. In fact this practice is quite general, not only for the garden, but also for lawns and on all hoed crops—in fields, lawns, and other places where it is practicable, we drive with carts upon which a barrel or cask is fixed, something like the sprinklers used in American cities. In small gardens, and places where it is impracticable to drive the liquid manure is applied by hand with sprinkling pots. In very dry seasons the liquid manure is diluted with an equal amount of clear water. In fact, when applied directly to the foliage, some water must always be added. It is applied on damp days, or immediately after sunset. Such manuring tells more promptly and effectively than any other.

That was 66 years ago. We have had in the last 15 years a reawakening with respect to the possibilities of applying nutrients to the above-ground parts of plants. In California and Florida we have thousands of fruit trees which are sprayed annually with many of the minor or trace elements.

In the northern parts of this country, and in certain European countries, apple trees are sprayed regularly with magnesium sulfate and urea nitrogen. In places where soil applications are not feasible or practical or are not useful, only the foliage applications give the desired response.

Thousands of acres of celery in the States of Michigan, New York, and Florida are being sprayed annually now with sprays of calcium and magnesium to correct certain nutritional disorders which are not easily corrected by soil applications, even when tremendous quantities were applied.

Also, in this country and in the Soviet Union, phosphoric acid has been used on an experimental scale over hundreds of acres of cotton to improve boll formation.

In the Hawaiian sugarcane plantations at the present time they are giving serious consideration not only to applying the trace elements, but the major mineral nutrients as well. This is an established practice with the pineapple people in those areas.

There are at this time millions of gallons of all-soluble liquid fertilizer being applied annually to the foliage of crops. Thousands of tons of all-soluble dry fertilizer are being sold for application in the

same manner, and one of the fascinating things which has developed in the past 5 years is that practically every major chemical and fertilizer company and a multitude of smaller ones who deal primarily in the business have a special product or formulation of soluble fertilizer which can be sprayed on the foliage of plants.

Representative PRICE. These are all chemicals now. What part does the isotope play in it?

Dr. WITTWER. We have been interested in evaluating the extent to which nutrients can be supplied to plants by means of spraying or dusting the leaves, and we are using isotopes, radiostopes, simply as a tool to follow the path of nutrients in plants, and by that tool we can ascertain to what extent that which is applied on the leaf is absorbed by the plant, and translocated downward into all parts of the plant.

With the first slide (exhibit 17), I will give an illustration of what happens. This is an autoradiogram of a squash plant prepared by a photographic film pressed against the plant which was treated with radiophosphorus.

EXHIBIT 17.—Autoradiogram of a squash plant harvested 48 hours after the first primary leaf (top leaf) was momentarily dipped in 25-milliomolar solution of o-phosphoric acid containing radioactive phosphorus (P^{32}). Note the transport and accumulation of meristematic tissues. Foliar applied phosphate is quickly absorbed and used in growth.

The top leaf was the portion of that squash plant which was sprayed with radiophosphorus and a few hours later that phosphorus has been absorbed by the leaf and translocated into the growing tips, the younger leaves, and down into the root system, just backward as to the usual manner in which nutrients are taken up by plants.

We find that the rate of translocation down the plant is to the extent of about an inch a minute, that is about 2 feet an hour. That is not quite as rapid as that for some of the nutrients that are applied to the soil and move in by the roots and are then taken up the plant, but we have very rapid movement by foliar applications.

We can trace the path of nutrients applied to any part of the plant and it is by the isotope technique that we are able to establish that that which was applied to the leaf has been absorbed by the plant and translocated to all parts of the plant and used in its metabolism. We find that very shortly, in a matter of minutes, after radiophosphorus, for example, is applied to the leaf we can separate from the plant organic phosphate compounds which are radioactive, showing that the phosphate is used quickly in the metabolism of the plant. There are other plants which show this same pattern. The highest concentration is in the younger tissue, in those plant parts which are growing most rapidly.

The isotope technique enables us to determine the mineral nutrient contribution in the plant that will come from any method of fertilizer application. We must keep in mind that in these studies and in the practical use of foliage sprays or nutritional sprays we need to know, or have some means of distinguishing nutrients which we apply to the leaf from those which are already in the plant, and which are being simultaneously absorbed by the roots. The isotope technique enables us to do this and evaluate the importance of the foliar spray method of fertilization.

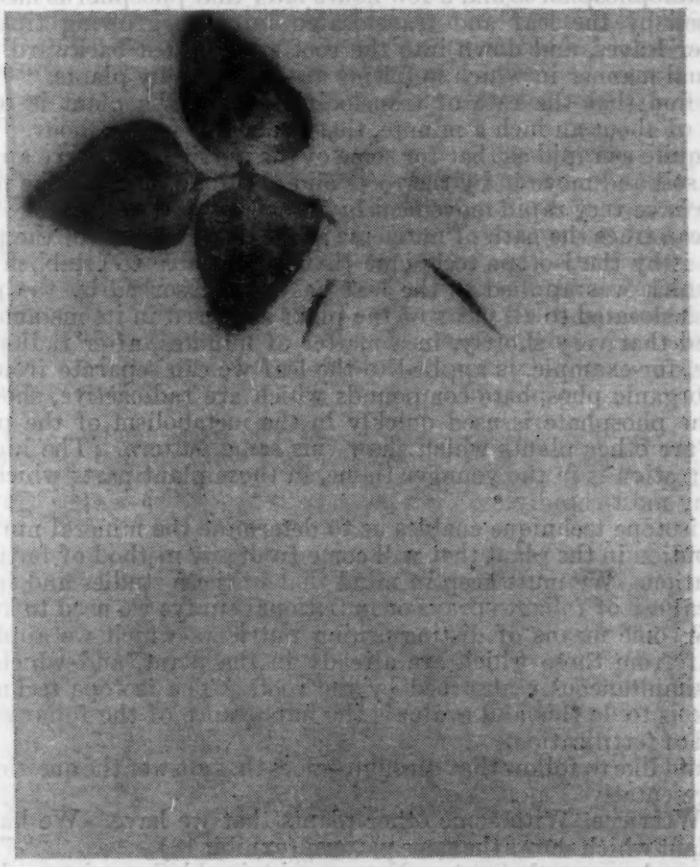
I would like to follow that through—does that answer the question?

Representative PRICE. Yes.

Dr. WITTWER. With some other plants that we have. We have a bean plant which shows the same pattern (exhibit 18).

Here we have another autoradiogram, obtained by pressing a photographic plate against the plant, showing the transport of radiophosphorus from the leaves down into the roots of a bean plant. Another interesting thing that the isotope technique has shown us is that the younger the leaf the more rapidly it absorbs the nutrient. We desired to know also if the top side of leaves and the bottom side of leaves would both absorb fertilizer, because in horticultural crops and in

EXHIBIT 18.—Autoradiogram of bean illustrating absorption and transport of P^{32} applied to the trifoliate leaf, and its later concentration in the young pods



many field crops we have leaf surfaces (exhibit 19) where the foliage forms a complete canopy over the soil and, in fact, in has been estimated with fruit trees, for example, we have tremendous leaf surfaces considering both top and bottom leaf areas.

Representative PRICE. What do the figures represent—0.104, and so forth?

Dr. WITTWER. Simply the amount in terms of micrograms found in the roots following application of the labeled phosphorus to the leaf. The amount in terms of micrograms 2 hours after treatment from that which was applied to the upper sides of the leaf, and to different parts of the bottom sides of the leaf. The figures show that the top sides of the bean leaf in this case absorbed radiophosphorus a little more rapidly than the bottom sides. Both sides, however, are effective.

EXHIBIT 19

Absorption of Ortho-Phosphoric Acid by Different Regions of Bean Leaves as Shown by Micrograms in Roots Derived From Solutions Containing P^{32} (2 Hours After Application)

Position on Leaf	Surface of Leaf	
	Upper	Lower
Tip	.104	.062
Margin	.130	.102
Mid-rib	.148	.104
Base	.206	.090
Mean	.147*	.090

* Absorption by upper surface significantly greater than lower ($P = 0.05$).

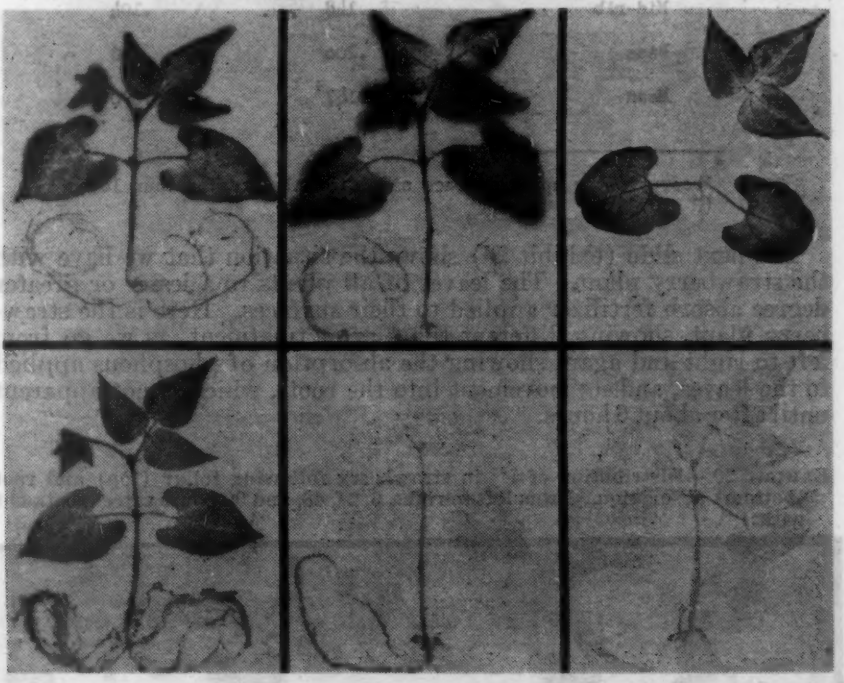
The next slide (exhibit 20) shows the situation that we have with the strawberry plant. The leaves of all plants to a lesser or greater degree absorb fertilizer applied to their surfaces. Here is the strawberry plant, showing different times after treatment, as we go from left to right and again showing the absorption of phosphous applied to the leaves, and its movement into the roots, which is not apparent until after about 6 hours.

EXHIBIT 20.—Distribution of P^{32} in strawberry following foliar (top) and root (bottom) absorption. From left to right, 6, 24, 48, and 96 hours after treatment with P^{32}.

In 24 hours, we see a sizable quantity moving into the roots from the foliage and into the fruit. Down on the bottom we have a comparison with the same time sequence on root uptake of the nutrient.

The next slide (exhibit 21) is an interesting one, because not always are all nutrients which are applied to leaves readily taken in and translocated and moved to other parts of the plant. On the left we have a bean plant in which the foliage was treated with radiophosphorus and the movement is apparent into the roots.

EXHIBIT 21.—Distribution of P^{32} (left), K^{42} (center), and Ca^{45} (right) in the bean plant following foliar (top) and root (bottom) applications. Autoradiograms prepared 48 hours after treatments were applied.



This is a root application of the same [pointing] mineral, labeled phosphorus. Here we have potassium applied to the foliage and it moves into the roots readily, and it moves from the roots into the top from root applications.

Over here we have calcium. Calcium applied to the leaves of the bean or to almost any other plant that we have been able to study is absorbed by the leaf, but does not move out of the leaf, and will not move down into the other parts of the plant, including the root, so we have here a situation where foliar applications of calcium wouldn't do much good as far as the root is concerned.

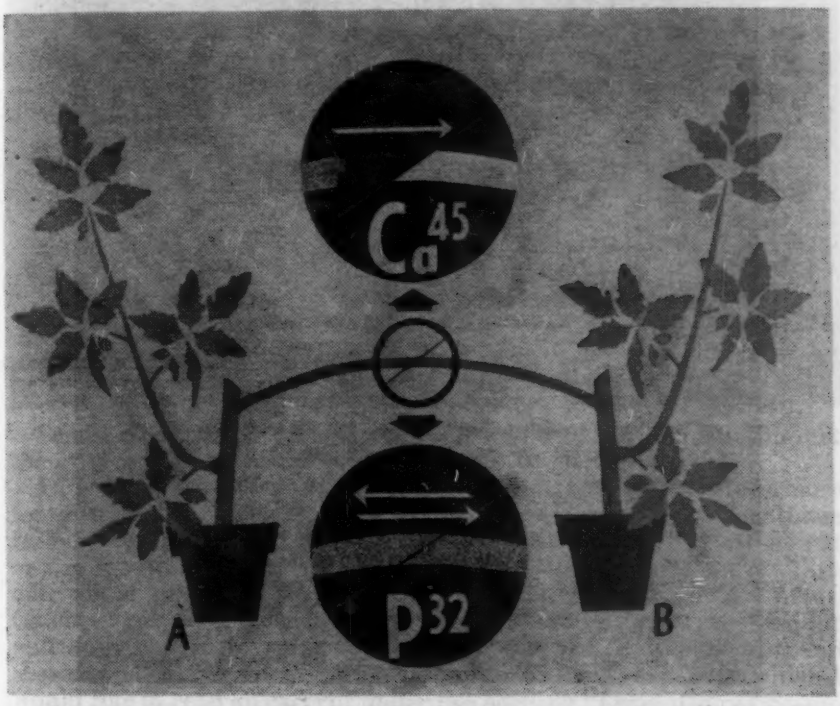
Down here we have a picture showing the movement of calcium up into the leaves. This movement of calcium in the leaves of a bean plant is extremely interesting as is its movement back and forth in plants.

Now, we are interested in this to evaluate the extent to which we can use various fertilizer elements in this method of fertilization.

The next slide (exhibit 22) shows the situation with calcium and phosphorous, both fascinating nutrient elements, very important in plant nutrition. Tomato side stems were grafted together against each other, and we applied calcium to the one plant and it moved to the graft union, but did not go into the other half.

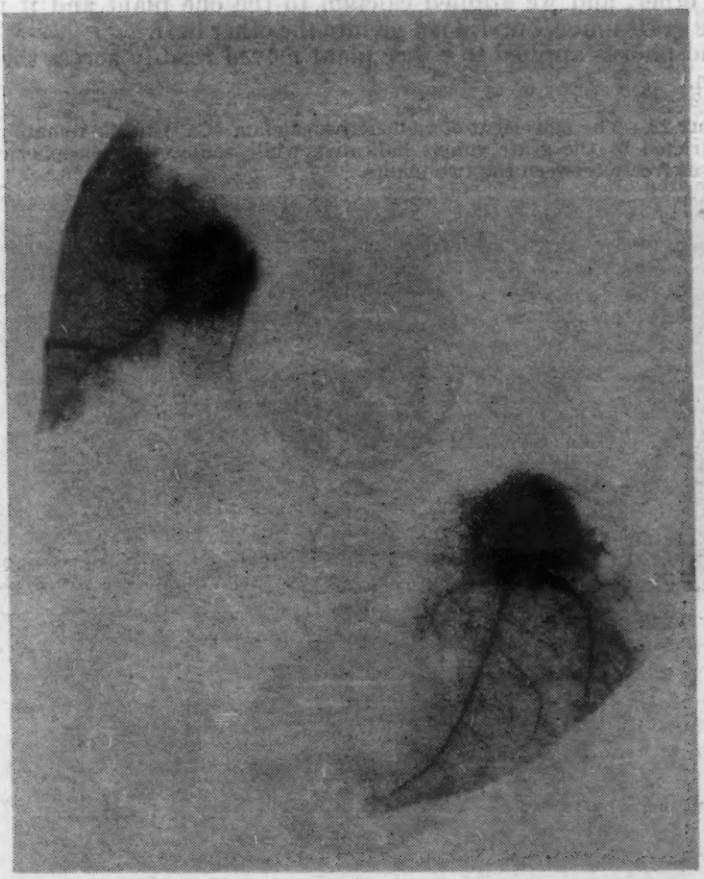
Phosphorus applied to either plant moved readily across the graft union.

EXHIBIT 22.—The movement of radioactive calcium (Ca^{45}) in the tomato plant is restricted by the graft unions indicated, while radioactive phosphorus (P^{32}) moves freely between the two plants.



The next slide (exhibit 23) shows another point. Here we can place a drop of radiocalcium on the bean leaf and we find very localized absorption and transport. It only moves toward the tip, and this has been very intriguing because we feel there is something here that deserves consideration.

EXHIBIT 23.—Radioactive calcium (Ca^{45}) placed as a drop on the surface of a bean leaf is readily absorbed but moves only toward the tip of the leaf. There is little or no downward transport of calcium to the roots from foliar applications.



Calcium is an important nutrient as far as plants are concerned, and the next slide (exhibit 24) shows another extremely interesting development.

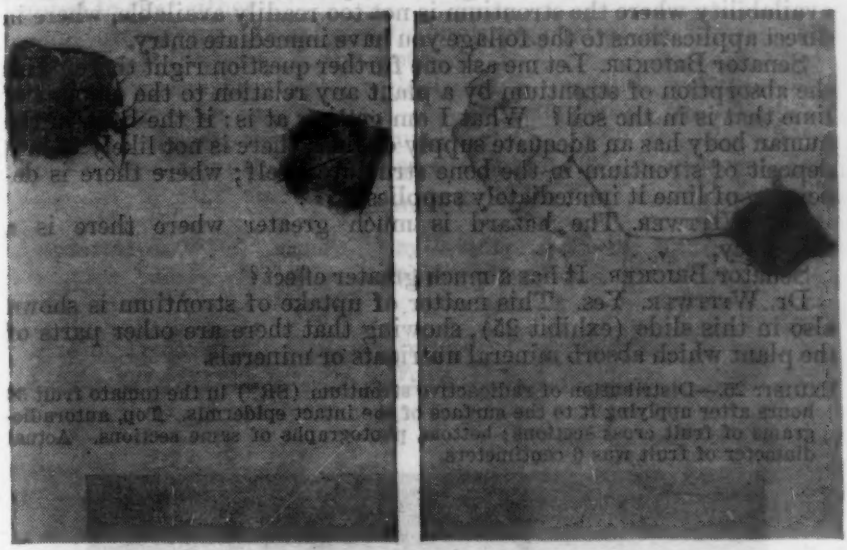
By subjecting plants to a mild anesthesia, very weak vapors of ether, we are able to apply calcium to the leaf of a bean plant and get it to move throughout the plant. We can, of course, study such phenomenon only by using radiocalcium, otherwise it would not be possible.

There are a number of interesting phases with respect to this calcium work that I would like to emphasize.

Senator BRICKER. Before you go into that, would not the conclusion necessarily be that your calcium will be more practically absorbed by the root system while the leaf will resist it more?

Dr. WITTWER. That is what I would like to emphasize and I appreciate your bringing that point out. However, where calcium is deficient in the foliage we have found even there a very practical instance in the case of celery, where it can be applied to the foliage to properly correct foliage disorders.

EXHIBIT 24.—Autoradiograms of bean plants showing the transport or radioactive calcium (Ca^{45}) from a local application on the upper surface and near the center of the primary leaf blades. Left, a normal plant showing acropetal transport only, and confined within the two primary leaves; right, active transport throughout the plant occurs if the leaf treated with Ca^{45} is subjected to low concentrations of ether vapor.



Senator BRICKER. This helps the general health of the plant, but not the growth?

Dr. WITTWER. It would not help the roots, but does produce more top growth. This has an interesting phase with respect to the atomic fallout, which I would like to mention briefly. We have a nutrient or a mineral element, strontium, a common constituent of atomic fallout, which follows the same pattern that calcium does in the plant. Calcium and strontium, chemically and physically, are very similar and their absorption by plants corresponds just about exactly, and there is an interesting report on fallout by W. F. Libby from which I would like to read an excerpt under the heading "Deposition of Strontium–90." I quote from Science, volume 123, page 659, April 20, 1956.

It descends—

speaking of fallout—

on the foliage and on the soil. That fraction of it which falls on plant leaves has a good chance of being absorbed directly into the plant—much in the same way that most modern leaf fertilizers operate. The Eniwetok tests were conducted on coral islands and as a result their fallout may be largely water soluble. In any case, direct measurements of the radiostrontium content of alfalfa and other crops showed them to be appreciably higher in radioactivity than the soils in which they grew, strongly indicating that a leaf assimilation mechanism is important.

And Scott Russell in England in another series of atomic tests found in other crops that the tops of plants were highly radioactive, but the roots were not.

This principle of the lack of downward transport of calcium and its close relative, radiostrontium, is interesting.

Senator BRICKER. That, however, does not apply to the immediate fallout because of the fact it goes into the soil more readily. It comes up again with a half life of about 27 years.

Dr. WITTWER. Twenty-eight years to be exact for strontium-90.

Senator BRICKER. So the first year you get it in the tips of the plant by the absorption of the leaf, and the second year coming through the roots which remain in the soil.

Dr. WITTWER. Yes, although in the soil there are problems of availability where the strontium is not too readily available, where in direct applications to the foilage you have immediate entry.

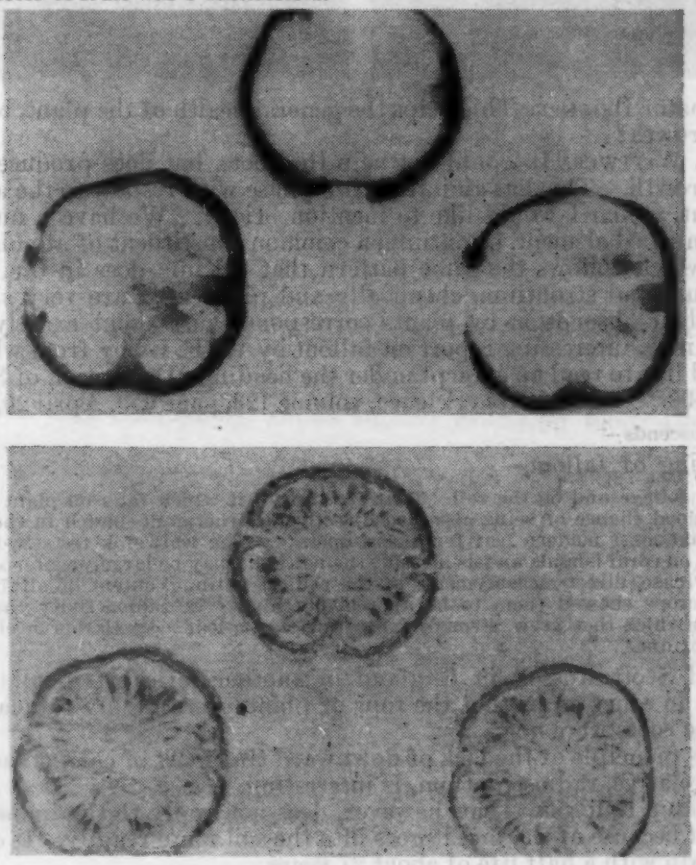
Senator BRICKER. Let me ask one further question right there. Has the absorption of strontium by a plant any relation to the amount of lime that is in the soil? What I am getting at is: if the bone in the human body has an adequate supply of lime, there is not likely to be a deposit of strontium in the bone structure itself; where there is deficiency of lime it immediately supplies it.

Dr. WITTWER. The hazard is much greater where there is a deficiency.

Senator BRICKER. It has a much greater effect?

Dr. WITTWER. Yes. This matter of uptake of strontium is shown also in this slide (exhibit 25), showing that there are other parts of the plant which absorb mineral nutrients or minerals.

EXHIBIT 25.—Distribution of radioactive strontium (SR^{90}) in the tomato fruit 36 hours after applying it to the surface of the intact epidermis. Top, autoradiograms of fruit cross sections; bottom, photographs of same sections. Actual diameter of fruit was 6 centimeters.



Here we have a cross section of a tomato fruit. This is an actual photograph of cross sections. Here are the same cross sections showing the distribution of radiostrontium as a result of direct absorption into the skin of the fruit, and so not only leaves, but fruit, absorb directly these materials which are sprayed upon them, and it is not limited to that either.

Senator BRICKER. It is taken through the rind of the fruit, rather than through the leaves or the root?

Dr. WITTWER. Absolutely, right through the rind, and in studies of this nature we have made a few estimates as to the quantities actually incorporated into the fruit.

The next slide (exhibit 26) shows stronium 89 and ruthenium 103.

EXHIBIT 26

Absorption Of Sr^{89} and Ru^{103} By Developing Tomato Fruit Following a Foliar Spray

Size of Fruit when Plants are Sprayed	Percent of Applied Radioisotope Found within the Fruit at Maturity	
(cm. in diameter)	Sr^{89}	Ru^{103}
1 - 2	2.5	1.5
5 - 8	3.4	0.4

These are the two constituents of atomic fallout which are absorbed in fairly large quantities by the plant, providing they are available, and up to almost 4 percent. Three and a half percent of these materials which will alight upon the foliage of plants will be found in the fruit 2 or 3 weeks later when the fruit is ripened, so it is a fairly good source of contamination.

Senator BRICKER. Strontium 89 and ruthenium 103 are both radioactive?

Dr. WITTWER. Yes.

Senator BRICKER. Both absorbed in about the same portion?

Dr. WITTWER. Yes.

Representative VAN ZANDT. As I understand your statement, radioactivity is brought to the fruit, through moisture?

Dr. WITTWER. That is a most interesting question. Moisture apparently is not necessary for the absorption of these minerals through the fruit or directly into the skin. You can spray it on and it will dry out in a few minutes, but absorption continues and continues and continues, even though the material and the surface is dry on the outside.

Representative VAN ZANDT. I am thinking of the radioactive fallout.

Dr. WITTWER. Some of the work of Scott Russell in England indicates after fallout dust falls upon the plants the nocturnal dews will dissolve it and then the radioactive substances enter the plant. It is an interesting fate of this absorption of nutrients by leaves and other above-ground plant parts.

The next slide (exhibit 27) has a great number of interesting aspects of this nutrient absorption by the leaves of plants and one of the most fascinating and exciting phases deals with how efficient is this method of the application of nutrients to the foliage of crops.

EXHIBIT 27

Absorption From Foliar Sprays As Percentage Of The Amount Of Isotopically Labeled Nutrient Applied

Plants Treated	Percent Absorption	Time for Absorption	Location
	Phosphorus		
Apple	32-48	7 days	New York
	75-100	30 days	New Hampshire
Bean, Squash	40-50	6 days	Michigan
Swede	50	10-12 days	England

Here we have some data assembled from various sections of the country including our own studies dealing with labelled phosphorus. By using radioactive phosphorus we can ascertain precisely how much of that which we apply on the foliage of a plant is absorbed and recovered in other parts of the plant at different time intervals after treating, and I might call your attention to some of these figures. This work was all done with radioactive phosphorus; otherwise we would not be able to arrive at such figures. Work in New York indicates that in 7 days 32 to 48 percent of that which was applied to the foliage of the apple was absorbed and used in the plant.

In New Hampshire work also with apples indicated in 30 days 75 to 100 percent, almost complete utilization, in that length of time.

With the bean and squash in Michigan 40 to 50 percent of that which was applied was absorbed within 8 days.

In England, work with Swedes, shows 50 percent absorption in 10 to 12 days. These are interesting figures because they show us that half time of absorption, is a matter of 7 or 14 days. Half of what is applied to the foliage of these crops in such a time interval is actually taken in and used by the crop.

Senator BRICKER. What would be the percentage in relation to that which you applied to the roots?

Dr. WITTWER. That is where the story comes in. Very detailed studies of the United States Department of Agriculture, in cooperation with various State experiment stations throughout this Nation, work in Canada, in India, and in other foreign countries indicate that that figure for the first season's crops averages or will range between 3 and 35 percent.

Senator BRICKER. Is that due to the lesser space in which to absorb, or is it due to the natural process of the plant growth?

Dr. WITTWER. In the case of phosphorus, it is a matter of phosphate being tied up in the soil and being diluted by the soil. There is no dilution in the case of foliar applications. The great limiting factor in this method of fertilization is that normally you cannot supply all of what the plant needs. You can supplement that which comes in from the soil, but in those crops which we deal with horticulturally—

fruit crops and others such as sugarcane and the pineapple—even with the major elements you can approach what the plant needs exclusively by this method of fertilization; and, speaking of economy of fertilizer usage, we have been able to establish that the most efficient method of fertilizer application in terms of phosphate is to apply it to the leaf, keeping in mind, of course, the limitation of the amounts that can be used.

Senator BRICKER. Then would you say, keeping in mind the figures that you gave me a moment ago from this soil absorption, that the process of fertilization in the field of phosphorus alone may be 10 times more efficient in the leaf application?

Dr. WITTWER. It would depend, of course, upon the soil type and the type of phosphorus used and the method of placement of the phosphorus in the soil, and, of course, the crop, but the usual figure as far as recovery of phosphate is concerned from soil applications is between 10 and 12 percent of that which is applied for the first season's growth. The half life of phosphorus would preclude normally determining what the effect would be in subsequent seasons and certainly there is some carryover in the soil which would be useful or utilized in subsequent seasons.

Senator BRICKER. The leaf there will run many times that?

Dr. WITTWER. With leaves, if we allow sufficient time and if weather conditions are such that this is possible, you approach almost complete utilization?

Speaking of the phosphate reserves of the Nation, which are limited, and the economy of fertilizer usage, we have something here to think about.

Senator BRICKER. Take this condition, Doctor, where there is an adequate amount of phosphorus for the growth of the plant in the soil, naturally in the soil, what effect would that have upon the percentage of absorption that was given to the leaf or sprayed on the leaf?

Dr. WITTWER. We have that information. It is in one of the slides which follows:

Senator BRICKER. I will wait for that.

Dr. WITTWER. I will mention that in just a moment.

Senator BRICKER. I was just curious.

Dr. WITTWER. I would like to show some figures on nitrogen and potassium (exhibit 28). With urea nitrogen in the crops which we

EXHIBIT 28

Absorption From Foliar Sprays As Percentages Of The Amount Of Isotopically Labeled Nutrient Applied

Plants Treated	Percent Absorption	Time For Absorption	Location
	Nitrogen (As Urea)		
Tobacco	25	6 hours	North Carolina
Tomato, Bean, Corn	100	3- 12 hours	Michigan
Celery, Potato	75	24 hours	Michigan
	Potassium		
Bean, Squash	25-35	72 hours	Michigan

have listed here, we have a situation in a matter of hours where over 50 percent of that which is applied is taken into the plant and very rapid utilization occurs. The half time figure for absorption is just a few hours in the case of this particular nutrient. In case of potassium we have values about the same as those for phosphorus, in terms of time with respect to absorption.

In the next few slides I think we will run into the one that the Senator wanted to see.

That is the one (exhibit 29). I would like to present to you a few factors which affect the absorption of mineral nutrients by leaves as we have studied them, with a limited number of plants, of course. We have the bean and the tomato and some data for tobacco which are not all of our own but represent that which we have assembled.

EXHIBIT 29

Effect Of Time Of Day On Relative Absorption Of Isotopically Labeled Nutrients By Plant Foliage

Plant Treated	Nutrient	Day	Night
Bean	Phosphorus	3	1
Bean	Potassium	1	1
Tomato	Phosphorus	2	1
Tobacco	Nitrogen (Urea)	1	5

Three times the absorption of phosphate by day over night occurs for the bean; about the same by day and night for the bean occurs with potassium. In tobacco, with urea nitrogen, five times the speed of uptake through the leaves occurs at night as compared to the day.

Representative VAN ZANDT. What is the reason for such differentials?

Dr. WITTWER. I don't know. Each time we run a study like this we would like to explore it further, of course.

Senator BRICKER. Had you used the nitrogen on the tomato and bean plants, would the same relationship of absorption of nitrogen be true in the tomato and the bean as is true in tobacco?

Dr. WITTWER. I would expect that it might be. I would expect that it would hold pretty well through various plant species, but I don't know. We, of course, are limited. There are many other variables which affect the uptake of nutrients by leaves. This is only one of them. The fertility at which plants are growing has a tremendous influence. I thought I had a slide on this but I do not.

We find the greatest uptake of phosphate where plants are grown at an average or medium level of phosphate in the soil. We find that phosphate absorption by leaves is reduced where phosphate levels are high in the soil and we find that phosphate absorption by leaves is reduced where phosphate is especially deficient in the soil. It seems

that phosphate deficiency changes the makeup of the leaf, and the leaf becomes more impermeable as a result of poor growth, so we find that halfway between we get the greatest utilization from foliar-applied phosphorus.

Senator BRICKER. Why is that?

Dr. WITTWER. We are not sure. There are more questions that we do not have the answers to than for which we have the answers. I was going to mention one more.

Temperature has a tremendous influence on the absorption of nutrient by plants. However, low temperatures are not as harmful insofar as reducing leaf absorption as they are in reducing absorption of nutrients by roots, and we feel that when plants are grown in cool soils in northern countries, foliage feeding is going to have tremendous possibilities where nutrient absorption is limited by cold soil, and often that is the case in the Northern States.

There are tremendous possibilities perhaps in the Arctic or near Arctic areas. This is a completely unexplored area so far. We have done only a little work in the laboratory in this connection.

Usually when sprays are applied to plants, various soaps, wetting agents or detergents and other additives are used to wet the leaves. In the work that we have done in this regard we have found in almost every instance, with the exception of this one product, sterox AJ, at one-hundredth of 1 percent, we get a reduction in uptake of phosphate when it is applied to the leaves (exhibit 30). We are not sure just why this is, but we find that where we use no wetting agent we get the most rapid uptake.

EXHIBIT 30

The Effect of Surface Active Agents on the Percent of Foliar Applied P^{32} Labeled Phosphorus Found in Stems and Roots of Bean Plants 8 Hours After Treatment

	Concentration		
Surfactant	0.01%	0.10%	1.00%
Sterox AJ	4.59*	3.44	1.57**
Triton B 1956	3.27	4.10	2.72
Glycerine	3.27	1.80**	0.97**
Tide	2.66	1.90**	0.20**
No surfactant added	3.30		

Differs significantly from control P=0.05*
P=0.01**

There is another factor tremendously important in the absorption of nutrients by leaves. I would like to show that in the next slide (exhibit 31).

EXHIBIT 31

Effects Of PH and Carrier Cation On Absorption and Transport Of P^{32} Labeled Solutions Applied To Bean Leaves. (% of Applied Phosphate In Stems and Roots 6 Hours After Treating)

pH	K	Na	NH_4
2	1.47	2.03	3.70
3	.96	2.97	3.94
4	.16	.31	1.59
5	.11	1.59	2.44
6	.41	1.21	.33
7	.80	.25	.26

It has to do with the alkalinity or the acidity, the pH, as we call it, of the applied solution, and also in this case we applied phosphorus as mono- or di-ammonium phosphate.

We find an interesting thing with phosphorus. We find that we get tremendously more rapid uptake at pH. 3 and with ammonium as the carrier. Of course, this has been found on field scale tests where it has been ascertained that phosphoric acid or the very acid solution of ammonium phosphate is the most suitable material for absorption of phosphate by leaves and this has been determined for a great number of plants.

Senator BRICKER. In addition to the absorption of the leaf in the fruit trees you have the absorption by the bark also, do you not?

Dr. WITTWER. I should have mentioned that. Perhaps I could dwell on that just a moment. Let me emphasize that all above ground parts of plants are capable of absorption of nutrients and as to particularly the bark and the twigs of fruit trees and shade trees and perhaps forest trees, the latter which we have not investigated, there are tremendous possibilities of applying fertilizer to these parts of the plants. There is a large surface area, and if fertilizers are applied to trees in the dormant stage, before the leaves come out in the spring but when the buds are swelling, you can use tenfold the concentration of fertilizer in the spray without injury, and this is one of the unexplored areas in which we need more information. We have done a little work with it. However, we need to evaluate those effects more precisely and extend our observations into other areas other than just the fruit trees that we have worked with.

If we add phosphate in connection with the herbicide and growth regulator, 2,4-D, we get an increase in uptake of phosphate in corn and beans. Ten parts per million of 2,4-D is most effective on beans and 100 parts per million on corn. As to the possibility of using

growth regulators to encourage the absorption of these foliar applied nutrients, of course we have only made a beginning and I show this information as just the first work which we have done in that connection (exhibit 32).

EXHIBIT 32

Effects Of 2,4-D On The Absorption Of Radiophosphorus By Bean and Corn Leaves

2,4-D (ppm)	Percent Applied to Foliage Recovered in Stems and Roots 6 Hours After Treating	
	Corn	Beans
10	.59	1.37**
100	.93**	.94
500	.48	.56
1000	.49	.54
Control (No Treatment)	.35	.72

** Significantly higher than control (P = 0.01)

Senator BRICKER. What do you depend upon to get this information out—the practical effects of it to the fertilizer manufacturer, and to the farm agents in the various counties; or just what method is used to get the research work down into the production program?

Dr. WITTWER. There are various methods, of course, which we use in an extension way, the radio, by distribution of literature, pamphlets, personal contacts with fertilizer companies, and conferences with growers.

I might say in this connection that we are the ones who are pressed for the information. It is most interesting.

Senator BRICKER. They are pressing you?

Dr. WITTWER. They are pressing us. Let me say this: that the grower, the farmer in this country, is somewhat forging ahead of the research work in this respect. They have used these materials.

Senator BRICKER. That is very interesting and very encouraging.

Dr. WITTWER. They have used foliage spraying. Commercial fertilizer companies and chemical companies are manufacturing the materials. Growers find that they get results. They want the information. It is a matter of us being a little slow in getting it out. We are limited but it is, however, a little encouraging also. We can hardly write fast enough to put forth this information to the folks that want it. This is a situation where it is being put into practice immediately and this has transpired largely within the past few years. There are products available. There are all-soluble liquid formulations, dry formulations, which are available. Growers are using them, almost any conceivable mixture for any purpose, and the last 15 years, has shown a 10-fold increase in the use of spray and dusting equipment and in the sale and manufacture of dusting and spraying equipment,

accompanied with rather remarkable engineering advances in the same area. To have spoken of this type of fertilization 15 or 20 years ago would have probably been somewhat foolhardy. There was neither the material nor was there the equipment of application nor the practice already in operation, but now we are the ones who are being pushed.

Senator BRICKER. I suppose the various communities are apprised and even the localized farmer is apprised by the extension agent to a degree? Most of them now have the information, I presume, that you are able to give, so that they could apply it in the most practical way to their particular communities and the particular farms in their communities?

Dr. WITTWER. That is true.

Senator BRICKER. I think agricultural agents need a lot of education.

Dr. WITTWER. We find that is quite true. We do a lot of extension work ourselves. Sometimes we have to sell our own program. We frequently do.

Senator BRICKER. Right to the grower?

Dr. WITTWER. Take it right to the grower. We do a lot of it. That is not unusual at all. It takes a little time, but I think it is time well spent.

Representative PRICE. Doctor, you are making available all those charts, are you not, for the record?

Dr. WITTWER. Charts?

Representative PRICE. Yes. Do you have the charts?

Dr. WITTWER. These can be supplied as well as the tables in the manuscript and I will see that they are included.

Representative PRICE. We would like to have those for the record.

Representative VAN ZANDT. Doctor, can you tell us what the conditions should be at the time you apply the spray?

Dr. WITTWER. Going back into that report about 66 years ago in the American Agriculturist, they knew a lot even then. They did not have the precise methods of determining just how well they could do these things, but they said that which was applied in the evening was more effective. They were dealing with nitrogen, say, probably in that liquid manure, and we find there is five times the urea nitrogen absorption at night as compared to the daytime. It does not always work that way with other nutrients. Phosphorus absorption occurs more rapidly in the daylight hours, but we would have to specify the nutrient and the plant. They differ so much. It is confusing. Sometimes we lie awake at night trying to figure out which one of these things we should do next, because they all need attention. This is a new area and isotopes have given us a unique tool that we have not had before to measure these variables.

We found and we early anticipated that if nutrients were taken up by the leaves of plants (exhibit 33), they could also be lost by the leaves of plants.

In other words, if they could move in they could move out. We subjected plants to simulated rainfall and determined the extent to which we could leach out of the plant radioactive nutrients which were previously absorbed by the root, and the traffic is two way as far as the leaf is concerned. Nutrients move in and out and perhaps

EXHIBIT 33

Loss Of Nutrients From Foliage Of Intact Plants Under Artificial Rain As Determined By Radioactive Isotopes

Plant	Percent Lost	Duration of Rain	Location
	Phosphorus		
Tomato	5.0	1/2 hour	South Africa
Potato, Corn	2.2-2.7	1/2 hour	South Africa
Rose	12.8	4 hours	Michigan
	Potassium		
Bean	5 to 71	4 hours	Michigan
	Calcium		
Corn	4	2 hours	Michigan
Squash	18	24 hours	Michigan

many of the nutrient deficiencies that we run into in plants in periods of heavy rainfall are those which result from the loss directly out of the leaf as well as leaching out of the soil. This isn't all our work. Some came from South Africa. Other folks had the same idea. A lady scientist down in South Africa came out with it about the same time we did. Five percent of the phosphorus which was previously absorbed by the root of the tomato plant was subsequently leached out of the leaves in one-half hour of rainfall. In the potato and corn, also in South Africa, 2 to 3 percent. In the rose, in Michigan, about 13 percent in 4 hours. That is the amazing thing: potassium, a 5- to 71-percent loss, depending on how the plant was grown, whether it was in light or darkness, or whether we have a high or low percentage of salt in the plant. We got this 71 percent loss when we subjected the bean plant to rainfall for 4 hours in the dark and when it had a high potassium level. Calcium also was leached from the leaves; 4 percent in corn; 18 percent in squash, in from 2 to 24 hours.

So we find as far as the isotope technique is concerned, nutrients can be taken up by leaves from spray solutions, and they can be leached from leaves by rainfall. We can trace their path through the plant. We know that they are utilized when applied in leaf sprays. We know that the efficiency of utilization far exceeds that in most cases, which is possible from soil treatments, and we also know that if they move in they also can move out.

Senator BRICKER. Of course, in that leaching through the leaf in rainfall, it would be redeposited into the soil?

Dr. WITTWER. Oh, yes, at least part of it. Some would be lost by runoff. Some of it would be fixed by the soil, and of course would not be available.

Representative PRICE. Thank you very much.

Representative VAN ZANDT. One final question, Doctor. Have you experimented to the extent that you applied the spray that passed the isotope or the radiation on to the plant from the leaf and at the same time you applied radiation to the root? I am trying to develop here which would take priority now. This is the $64 question.

Dr. WITTWER. Of course, our interest is in foliar absorption, and it is possible to use different isotopes to apply, say, radiocalcium to the leaves and at the same time apply radiophosphorus to the roots. You could distinguish these two in the plant in radioactive analysis because they would have particles emitted differing in penetration. Half lives are also different, but we could not study application of radiophosphorus to both the leaves and roots at the same time, because we would mix them up in the plant and they would be indistinguishable, but where we use radioactive nutrients emitting particles differing greatly in physical properties we can determine, of course, what happens.

Representative PRICE. Thank you very much, Dr. Wittwer.

Dr. DUNHAM. Mr. Price, the next scientist who is going to present a report is Dr. Melvin Calvin of the department of chemistry and radiation laboratory, University of California, Berkeley, Calif. Dr. Calvin is probably the outstanding student of the process of photosynthesis that this country has ever produced. Dr. Calvin is going to talk about photosynthesis and other related biochemical subjects.

Representative PRICE. Dr. Calvin.

STATEMENT OF DR. MELVIN CALVIN, DEPARTMENT OF CHEMISTRY AND RADIATION LABORATORY, UNIVERSITY OF CALIFORNIA, BERKELEY, CALIF.

Dr. CALVIN. You have heard in the course of the morning a description of a variety of ways of getting nutrients into plants, among other things, and some of the factors which limit the way in which these nutrients are absorbed. It is perhaps worth mentioning that the reason that the plants need these nutrients is that they have to accomplish their primary function of converting the carbon either from the air or, as Dr. Thorne mentioned, from the roots in the form of its lowest energy condition as carbon dioxide into some sort of useful potential energy such as sugar, or protein, or fat, as the case may be.

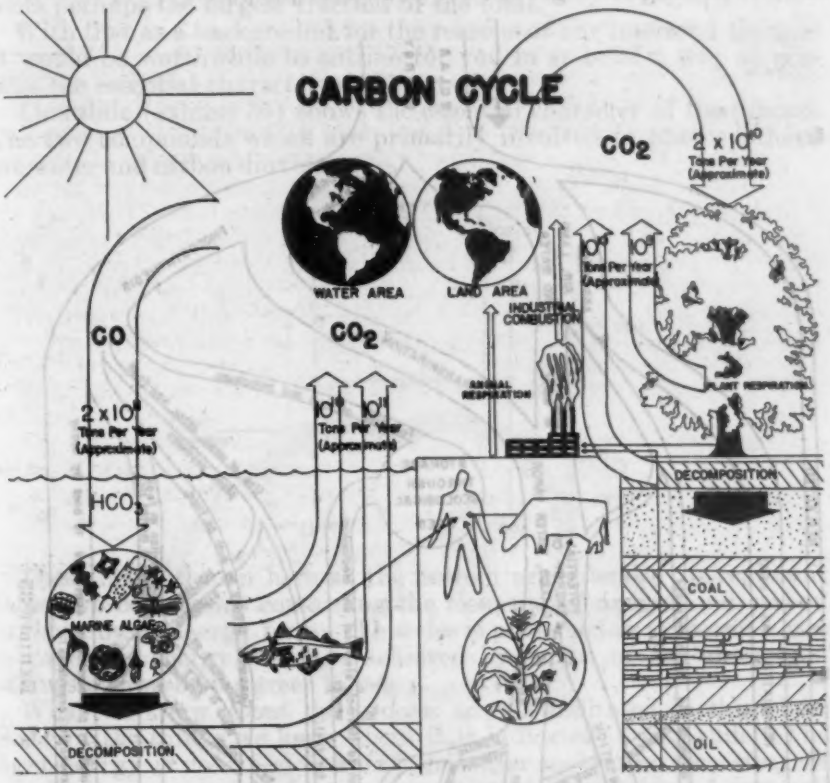
The process of doing this, which all green plants employ, is called photosynthesis, and truly all agriculture, all agriculture, begins with photosynthesis.

It is quite easy to outline for you some of the reasons why we have been interested in this and give you some indication of the ways that we have employed in trying to get some information about the process. One can go one step further back even and point out that all life, not just agricultural life, but all life, is dependent upon the ability of green plants to transform the solar energy into chemical energy, and this is really the problem with which we are concerned.

It is not merely a problem of transformation of energy, but a transformation of substance as well. All living things are made up of

the atom, or element carbon, as their primary constituent, and the first slide shows the relationship of the carbon on the surface of the earth, the carbon cycle, as we roughly estimate it.

EXHIBIT 34



This represents the amount of carbon (exhibit 34) that is taken from the form of its lowest energy, the form that is carbon dioxide, into higher potential energy, and this is about 2 times 10 to the tenth power tons per year. On the land area of the earth roughly that amount of carbon is transformed from the form of gaseous carbon dioxide, which is a carbon in its lowest energy form, into reduced carbon in the foliage plants. This in turn then is returned to the atmosphere by the respiration of plants, by the respiration of marine animals, or after their death by decomposition through micro-organisms. In both cases, as well as in the case of the land plants, the decomposition results in the formation of fossil fuels such as coal and oil. The carbon that man uses is derived from three principal sources. It is all derived from photosynthesis, but you can see now the route by which it is derived. Man eats most animals and vegetables, but in both cases the animals which he consumes in turn must subsist on the vegetable life which is the only form which can convert the carbon from CO_2 into something useful. This gives some idea, then, of the flow of carbon on the surface of the earth.

The next slide (exhibit 35) gives us a brief sketch of the flow of energy. There is the influx of solar energy. Most of it is not used for any useful purpose and is degraded and reaerated. A relatively small amount of it is used by plants in photosynthesis, and of course most of it is again degraded for nonuseful purposes.

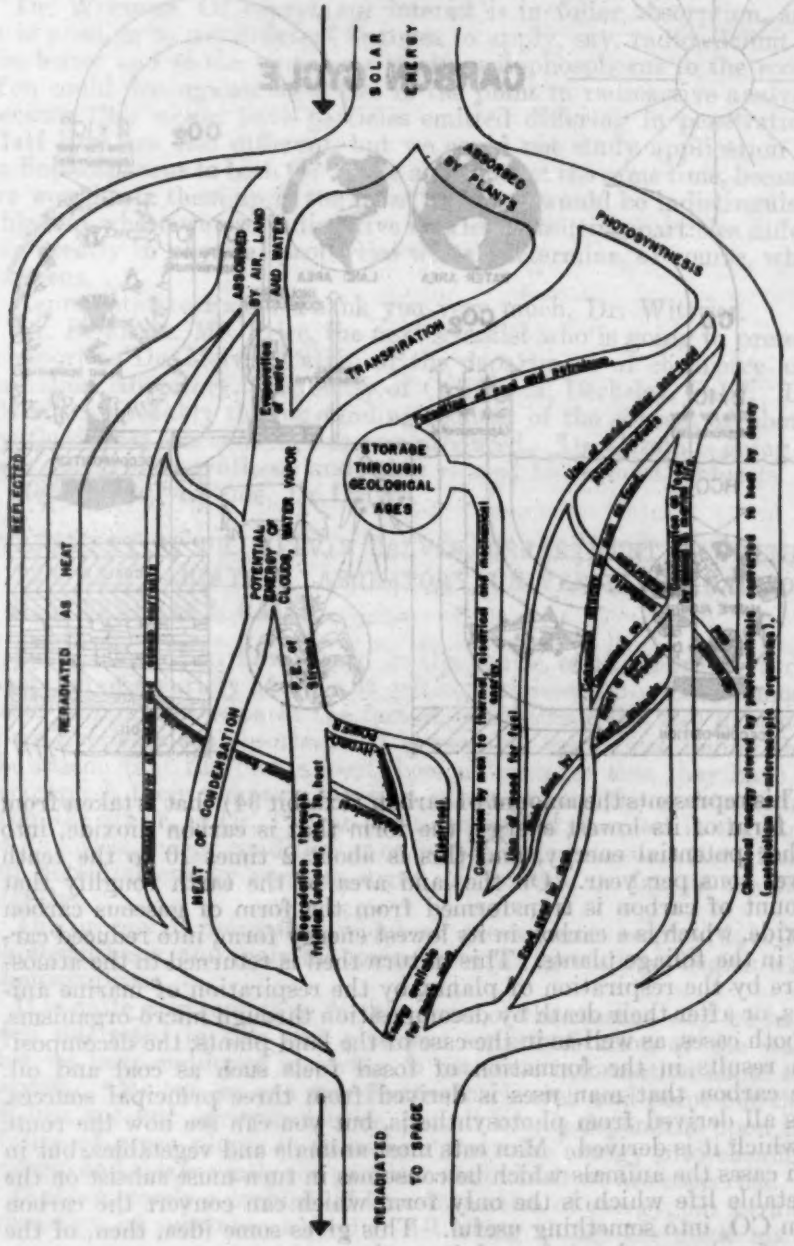


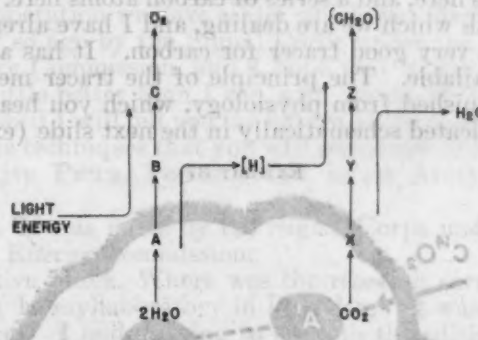
EXHIBIT 35

The useful purpose to which the photosynthetically captured energy is put is shown in this part of the chart. This is food here and this represents energy, which is the sum of annually produced energy, such as wood, and fossil energy such as coal and oil, and this represents perhaps the largest fraction of the total.

With that as a background for the reasons of our interest I thought it would be worthwhile to outline for you in as brief a way as possible the essential character of the process.

This slide (exhibit 36) shows the essential character of the process. The two compounds which are primarily involved in photosynthesis are water and carbon dioxide.

EXHIBIT 36



These being drawn here at the bottom are intended to represent these two compounds containing the elements of oxygen and carbon in their lowest energy form. This rise is presumed to represent a rise in potential energy which is achieved by virtue of the absorption of the sunshine by the green leaves.

What we know about the process now is indicated in this slide. Some of the things we know about it is indicated in this slide. The light energy is used first to break the water molecules, consisting of two hydrogen atoms and an oxygen atom into something I just call A, B, and C, because we don't know what they are, eventually becoming the molecular oxygen of the atmosphere which we must have for breathing.

The other two atoms, the hydrogen atoms, are broken off from the water into some active form represented by this H and they then move over in the green part of the plant to operate on some materials which are formed from the carbon dioxide, which is absorbed through the leaves, and sometimes through the roots. Here again we have a series of X, Y, and Z, indicating the beginning of this work on unknown materials. This formula represents the sugars which are the primary products of this process.

You can see how the availability of isotopes makes possible an investigation of this process. As a matter of fact, it is the only way in which this process can be investigated. The availability of radioactive carbon, carbon 14, which came to us in 1945 or 1946, right after the war, in relatively large amounts, because of the existence of reactors, made possible the tracing of this roadmap.

Senator BRICKER. Have you been able to learn anything about the nature of X and Y and Z?

Dr. CALVIN. This is the burden of my discussion this morning.

Senator BRICKER. Excuse me. Go right ahead.

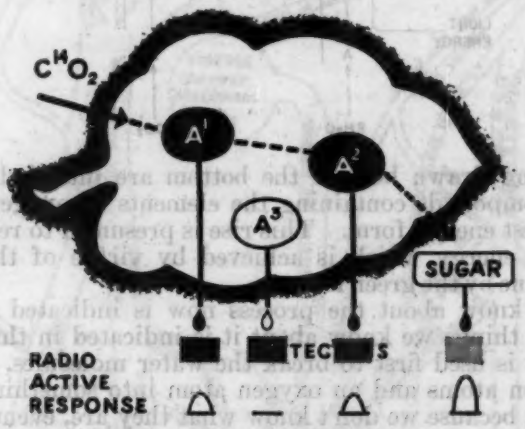
Dr. CALVIN. I might as well tell you right now we can draw that roadmap completely for the first time this year.

Representative PRICE. Doctor, you said for the first time this year. You mean this is a very recent development?

Dr. CALVIN. I think that the first announcement of it in its present form was at the Geneva meeting last summer. We have changed it a little bit, modified it a little bit in the last 2 or 3 months, but the essential features are fixed now. We will come back to this in a moment.

I want to keep you apprised of the relationships of the atoms that are involved here. There is a series of oxygen atoms here, a series of hydrogen atoms here, and a series of carbon atoms here. These are the three atoms with which we are dealing, and I have already mentioned that we have a very good tracer for carbon. It has a long life and lots of it is available. The principle of the tracer method in chemistry as distinguished from physiology, which you heard earlier this morning, is indicated schematically in the next slide (exhibit 37).

EXHIBIT 37



Here is a diagram of a leaf. The carbon is entering and eventually becomes sugar. The problem is what are these things in between the carbon dioxide and the sugar? The way it is done is to get a plant growing and doing this job with ordinary carbon, and then at a given instant of time you slip into this stream of carbon that is entering the leaf and going into sugar some of this tracer. After a few seconds or minutes, as the case may be, you take the leaf of carbon or plant, whichever plant we happen to be using, and examine the various compounds to see if they are radioactive in order to determine whether or not they lie on this road between the carbon and sugar. This diagram is to show how we do it.

We pull out compound A^1 here and put it on a Geiger counter to see if there is radioactivity. We pull out A^3 and put it on the Geiger counter and see if there is radioactivity, and there isn't, so we know that compound A^3 is not on this roadmap. Compound A^2 does have it, and so on along the line.

In the course of time first the carbon will get into this one, and then the next one and the next one and the next one and we did, by a series of time exposures, flash snapshots if you like, trace this road-map from carbon dioxide to sugar.

Representative VAN ZANDT. When did you get your first indication of sugar?

Dr. CALVIN. It depends on how much sugar you are looking for. The amounts that we look for can be found in a few tenths of a second. It also depends, of course, on the plant and its state of nutrition and so on, but in general, a few tenths of a second is all that is necessary for the formation of sugar.

Senator BRICKER. Your carbon 14 reacts precisely as well?

Dr. CALVIN. Yes. In order to give you a better idea of all of the stages in this operation we have a film which was made in our laboratory a year or so ago by the Signal Corps under the auspices of the Atomic Energy Commission, and I hope that it will show you how we do this a little better than I can with words, if it works. When the film is finished I will tell you the nature of the results that we have obtained by the techniques that you will see demonstrated on the film.

Representative PRICE. You say this is an Army Signal Corps picture?

Dr. CALVIN. It was made by the Signal Corps under the auspices of the Atomic Energy Commission.

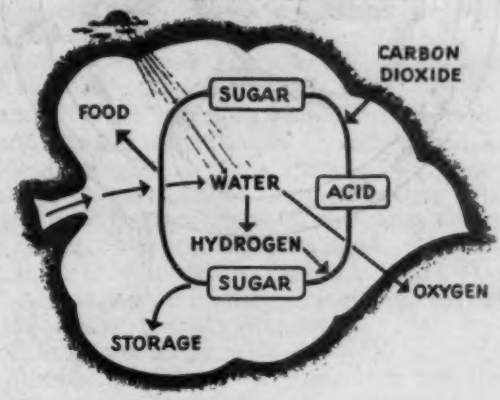
Representative PRICE. Where was the research carried on?

Dr. CALVIN. In my laboratory in Berkeley. It was edited by some Hollywood firm. I had nothing to do with the editing.

(At this point the film, The Riddle of Photosynthesis, was shown.)

Dr. CALVIN. I thought perhaps I had better narrate a little bit about what we could do, now that you have seen what the technique of the development is. What we have learned by this technique is shown in the next slide (exhibit 38).

EXHIBIT 38



This pathway now which you saw elaborated by means of these various spots can be now mapped, and here is the first simple diagram of what this sequence might be. Here again is the diagrammatic map, the leaf, the carbon dioxide entering the left, the sunshine decomposing the water and making active hydrogen and oxygen. The hydrogen

is used to convert the first product which is an acid formed from the carbon dioxide and a sugar, from the acid to another sugar. Some of these sugars are stored. Some of them are used as plant food, and some of them are used over again to take in more CO_2. This is the simplest schematic representation of two most important compounds, the acid and two of the sugars.

The last slide (exhibit 39) shows the same thing, but a little more detailed; the sun's energy comes in, and is absorbed by the chlorophyll, which then in turn decomposes the water into some active hydrogen and something which eventually becomes molecular oxygen.

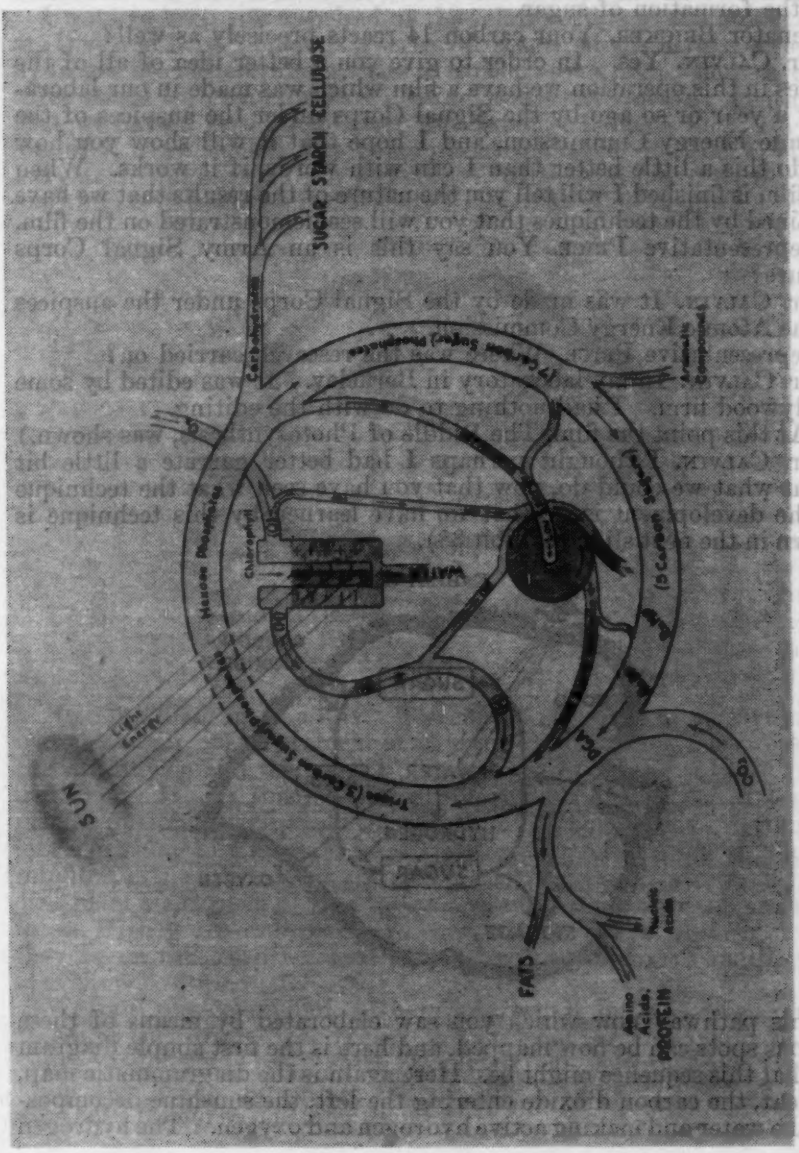


EXHIBIT 39

This active hydrogen reduces or reacts with the initial acids that are formed when the carbon dioxide is absorbed, and these things then are sugars going around in a cyclic system of this sort.

In addition to the active hydrogen that is required to convert the initial acid to sugar, we need some special phosphorous compounds.

You heard a great deal about the need of phosphorous fertilizer. This is why we need it, for what it does in the plant, or at least one of the things it does. It is essential for the conversion of the initially formed acid to sugar. In order to make this special form of phosphorus we have to reburn some of this active hydrogen and some of this intermediate oxygen to raise the ordinary phosphorus as it comes in from the fertilizer into the special high-energy form. This means then it keeps going around and around and, as you see, every time it goes around it takes in one atom of carbon. One can take off of this cycle chemicals for various purposes. At this point one can take off the carbohydrates which go into sugar, starch, and cellulose. Sugar is stored in sugar beets. The cellulose, which is a wood substance in the starch also forms in the granules. Other types of organic compounds can be taken off at different points of the cycle.

Here, for example, fats can be taken off, here proteins can be taken off, and here the essential constituents of the chromosomes which carry the genetic substance of plants and various other such points of removal are being found.

What we have done up to now is to draw the primary road map here. We are only beginning now to investigate these points of departure. You can see that one of the things that we can do now, now that we know every step in this sequence, is to begin to manipulate it a little bit. We can actually change the rate or amount of the various products which a particular plant will form.

Just the other day we were able to find a chemical which would increase the rate of sugar formation in some plants by a factor of 2 or 3. This is the beginning of this kind of manipulation of the nature of what the plant can make. There are other possibilities which will obviously come forth later.

We must further investigate how the other compounds are manufactured.

Senator BRICKER. Have you been able to increase the protein production in plant life to the extent where it would affect the feed content or the feed value?

Dr. CALVIN. Oh, yes; we can do that. Whether it is economically feasible or not is another question. That same thing is true with sugar. I mean this work is at a different level.

Senator BRICKER. It is not in the practical field?

Dr. CALVIN. No; it is not in the agricultural experiment station. It is in the realm of what we call science.

Senator BRICKER. Basic science?

Dr. CALVIN. Yes; that is right. It has to go from here to the agricultural experiment stations and then on out to the field.

Senator BBRICKER. They are doing a lot of that with the knowledge that has already been ascertained?

Dr. CALVIN. Yes; which is already on its way.

Senator BRICKER. In the field?

Dr. CALVIN. Yes. It is already on its way. You have seen what we have done with this road map and what has become of it. It has

become a rather complex cycle of carbon compounds, and we are only now beginning to learn how to manipulate this cycle.

We know, for example, where the essential nutrient, fertilizer phosphorus, plays its part, where the iron plays a part, where the magnesium plays a part, and there are many other substances whose functions we are yet unaware of and which are being used.

There remain two other rather obvious problems that we must attack. Just as we have traced with the tracer isotope this route and are beginning to find the branchings for useful products later on, so we must know more about this. You see, I have not said anything yet about how the light energy is primarily converted, and we do not really know this. One way of approaching this will be to map the road of oxygen from water to molecular oxygen. The first experiment of this sort was done also in Berkeley some 20 years ago with isotopic oxygen, and it was determined that the gaseous oxygen which comes off from the leaf has its origin in the water and not in the CO_2.

There are oxygen atoms in both, but this one comes from here, and not from here. What happens in between has not been determined. One of the reasons that it has not been determined is that we have no useful radioactive isotope of oxygen, and we must, therefore, use concentrated rare isotopes. These are the oxygen isotopes 17 and 18.

Senator BRICKER. They are not radioactive?

Dr. CALVIN. They are not radioactive; no. These occur in nature. Unfortunately, they are not very plentiful, and, in fact, we must import today the heavy oxygen that we use, and, even so, it is not available in our country at the levels that we would like to have it.

The other is the difficulty of using it. It is not radioactive. It requires a special technique, not the kind that we have shown here, but another one involving the use of mass spectroscopy and an entirely new type of development which will permit us to do almost this kind of measurement, depending upon the nuclear spin, the spin of the nucleus. The nucleus is a little spinning thing, and we can use the nuclear spin of one of the heavy isotopes of oxygen, oxygen 17, to follow it around.

Senator BRICKER. How do you get those heavy isotopes?

Dr. CALVIN. This is a great problem. Right now we are importing this.

Senator BRICKER. From where?

Dr. CALVIN. The only country that has them for sale is Israel. The other one that has them, but not for sale, is the U. S. S. R.

Senator BRICKER. How are they produced?

Dr. CALVIN. By water distillation. At least the Israeli plant is water distillation and the one that I saw in Geneva as a model that the Russians had there was also a water-distillation plant. I am not sure that this is the best method, but it is the only one that I know of that is available for quantity production today.

Representative VAN ZANDT. Are we making any effort to produce that here?

Dr. CALVIN. I think Dr. Dunham might answer that.

Dr. DUNHAM. They are working on the problem at Oak Ridge in their stable isotope program. I do not know how far along they have gotten.

Representative VAN ZANDT. Have we a use for them in other fields?

Dr. DUNHAM. All through the biological sciences a useful tracer isotope of oxygen will be valuable whether it is dealing with such things as carbohydrate metabolism in diabetes, or fat metabolism, a lot of things in medicine as well as in these fundamental studies with photosynthesis and in agriculture generally.

Dr. CALVIN. After all, you breathe it all the time, and the question of how it is used in animal life and how it is produced in plantlife are very closely related questions. I am speaking now of the question of how it gets from water to molecular oxygen.

Dr. Dunham has just mentioned the reverse process, how it gets from molecular oxygen back to water when the animal uses it, and they are very closely related. They are certainly not identical, just as the path of carbon from CO_2 to carbohydrate in plants is not the same as the path of carbon from carbohydrates back to CO_2 in animals. They are not the same process.

Also we would like to be able to trace this, and this we are just beginning to do with the ready availability of large amounts of D_2O. That is heavy hydrogen material. On large scale we can grow plants practically, and we have just begun to do that in order to get some ideas about the nature of this route.

These are some of the remaining problems. We could outline a few more. I think perhaps this one would be worth saying a few more words about. I described here this matter of hydrogen and here is the path of oxygen, which we do not know anything about. Right in the middle here I have schematically drawn a bit of greenstuff, which you will recognize as chlorophyll, and around it are water molecules. Somehow the electromagnetic energy of the sun is absorbed by chlorophyll to make an excited chlorophyll on it. What happens after that instant we do not know. Somehow that excited chlorophyll molecule with its electromagnetic energy which is taken from the sun decomposes water. It changes water from the low-energy condition that it is in here into some active hydrogen and some active oxygen, the nature of which we do not know, and I believe that by approaching this problem from both sides, from both the hydrogen material side and the oxygen side, we will be able to come closer to the nature of this fundamental process.

In addition to that I think we must apply the newly developed physical and chemical methods to the process itself. This involves rather special equipment and special types of examinations.

For example, we can look at the color of the chlorophyll molecule as a function of it, depending on how fast it changes. We will illuminate it, shine a bright flash of light on it, and see the color of the chlorophyll change.

Senator BRICKER. That is the field they are working in in Antioch, in Dr. Kettering's laboratory?

Dr. CALVIN. Yes; not quite that way. They have been working there for quite a long time more on the chemical nature.

Senator BRICKER. They have not been using isotopes?

Dr. CALVIN. No; not at all. They have been working on the flash experiments that I have just described. These are entirely new. They have been working more on the nature of the chlorophyll molecule itself, not so much on its photochemistry and how it behaves, but they have made considerable progress in that direction.

I feel that we must apply the new physical and chemical methods which have been made available to us in the last few years to this problem of the primary act in much the same way that we have applied the isotopes to the tracing problem which I have already described to you.

One can go on and describe these things in detail, but I feel that we would not do much more than to list all of the unknown factors as they now stand, and there are many of those.

Representative VAN ZANDT. Doctor, how long has it taken you to develop the road map?

Dr. CALVIN. Of the carbon?

Representative VAN ZANDT. Yes.

Dr. CALVIN. During the war years I was busy with plutonium extracting processes. In December of 1945 that pressure was released, as you know, and in January of 1946 this work began. The cycle was first completely visible to us in 1955. We modified it a little bit. It is 9 years. We modified it a little bit this year, but it has now been done.

I might say that that manufacture of sugar from carbondioxide and water has actually been carried out in the absence of green tissues, or, I should say, of any particle of a living plant, so this was done last year.

Senator BRICKER. When these unknowns are finally determined you will be much closer to the understanding of the live process?

Dr. CALVIN. Oh, yes. These things are all associated, the mechanism of the energy conversion process and the mechanism of the synthesis of nucleic acid, which I mentioned here, the mechanism of the protein, which we have just been getting into now. Now that this is mapped we are going to go on in this direction and this direction and ths one and other ones. As we get those things understood we come closer and closer to joining hands with the microbioligist, on the one hand, for example, with the geneticist on the other other, with medical people on the third, and so on. They are things that are all part and parcel of one and the same thing, namely, the nature of life itself.

Representative PRICE. Doctor, you say you got sugar. How would it compare with the normal sugar that is grown in the field?

Dr. CALVIN. It is exactly the same.

Representative PRICE. Exactly the same?

Dr. CALVIN. Yes. That is what we investigate.

Representative PRICE. With all the same properties?

Dr. CALVIN. Yes, sir. Our problem was to find out how a plant does this very thing, make normal sugar in the field. That is the essence of it.

Representative VAN ZANDT. Doctor, in the future do you think it may be possible to control the amount of sugar?

Dr. CALVIN. Yes; I think that will certainly be possible. It fact it is already possible. As I mentioned a while back, by a suitable chemical we can change the rate at which the plant makes sugar. We have been able to, for example, just last month increase the rate of formation of sugar in a particular plant by a factor of three. What it amounts to is closing down one of these little gaps and opening up this one so that more leakage goes here instead of there, and we have been able to do that.

Senator BRICKER. How soon do you think you will reach the point where you can produce synthetically your organics out of your inorganic material?

Dr. CALVIN. We can do it now in the absence of chlorophll.

Senator BRICKER. In the laboratory?

Dr. CALVIN. In the laboratory; yes. It has been done, in fact, by, as a result of our work, defining each one of these steps, making it possible to take the catalyst, the enzymes, separately, put them all together, add carbon dioxide and this active hydrogen compound and the active phosphorus compound, and the thing goes.

Senator BRICKER. It comes out as carbohydrates?

Dr. CALVIN. Yes.

Senator BRICKER. That has a great potential for the future, has it not?

Dr. CALVIN. It is hard to foresee what the fundamental knowledge will do in any particular instance, but one thing I can say with a great deal of certainty is that as this kind of fundamental knowledge and any other, for that matter, accumulates it will have a profound effect on our mode of living. That is a statistical certainty, if you understand what I mean, but particularly which application it will be, that is not possible for me to say. That remains for the agricultural experiment stations and the people to develop and they will do so. I have every confidence that they will.

Representative VAN ZANDT. Doctor, is it firmly established that without the radioactive tracer it would be impossible?

Dr. CALVIN. Yes, sir. As a matter of fact, the argument as to what this was had been raging since 1860, so you see it was going on for almost 90 years, something of that sort, before we were able to draw the map.

Representative PRICE. It took you 9 years to find out?

Dr. CALVIN. It took us 9 years after we got the isotope in large amounts, that is right. I mean easily available.

Senator BRICKER. There is no radioactive isotope of hydrogen, is there?

Dr. CALVIN. Yes; there is tritium.

Senator BRICKER. Can it be used?

Dr. CALVIN. Yes; it can be used. There is a disadvantage in using it, although we have used it. The disadvantage is that whereas the isotope of carbon, carbon–14, has a weight of 14 units, it differs from the normal isotope which weighs 12 units, by only 2 parts in 12, so that the behavior is very much the same, but tritium has a weight of 3 units and normal hydrogen has a weight of 1 unit. It differs by 300 percent and the behavior is sufficiently different so that at least is one deterrent toward using it as a tracer, because that great difference in chemical behavior does show up. That is, after all, a 300 percent difference.

Representative PRICE. Are there any further questions?

Senator BRICKER. I would say it has been the most fascinating presentation that I have listened to in a long time.

Representative PRICE. It was a very fine presentation, Dr. Dunham. We certainly appreciate your efforts that you put into the selection of your witnesses and the material which has been shown here this morning. I imagine you will continue tomorrow.

Dr. DUNHAM. Yes, sir; we will be here with some other witnesses at 10 o'clock.

Representative PRICE. The committee will meet again tomorrow morning at 10 o'clock. Thank you very much.

(Whereupon, at 1 p. m., Monday, June 4, 1956, the hearing was recessed until 10 a. m., Tuesday, June 5, 1956.)

PROGRESS REPORT ON RESEARCH IN MEDICINE, BIOLOGY, AGRICULTURE, AND FOOD PRESERVATION

TUESDAY, JUNE 5, 1956

CONGRESS OF THE UNITED STATES,
SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT,
JOINT COMMITTEE ON ATOMIC ENERGY,
Washington, D. C.

The subcommittee met at 10 a. m., pursuant to recess, in room P–63, the Capitol, Representative Melvin Price (chairman of the subcommittee) presiding.

Present: Senator Bricker; Representatives Price and Van Zandt.

Representative PRICE. The committee will be in order.

This is a continuation of the hearing that was opened yesterday by the Research and Development Subcommittee of the Joint Committee on Atomic Energy to receive progress reports on the uses of atomic energy for research in the fields of biology, agriculture, and food preservation.

Dr. Dunham, I think we will follow the same procedure we followed yesterday, if you will be so kind as to present those who will testify. Will it be food preservation this morning?

STATEMENT OF DR. C. L. DUNHAM, DIRECTOR, DIVISION OF BIOLOGY AND MEDICINE, UNITED STATES ATOMIC ENERGY COMMISSION

Dr. DUNHAM. Yes. Dr. Schweigert, assistant director of research and education of the American Meat Institute Foundation, and associate professor of biochemistry at the University of Chicago, is going to report on the use of ionizing radiations in food preservation.

Representative PRICE. Dr. Schweigert, will you present your testimony?

STATEMENT OF DR. B. S. SCHWEIGERT, ASSISTANT DIRECTOR, RESEARCH AND EDUCATION, AMERICAN MEAT INSTITUTE FOUNDATION, AND ASSOCIATE PROFESSOR OF BIOCHEMISTRY, UNIVERSITY OF CHICAGO, CHICAGO, ILL.

Dr. SCHWEIGERT. Mr. Chairman, the food industries are constantly looking for improved methods of preserving food, and it has a very great importance to agriculture to conserve the food that is produced. The conventional processing methods that have been in use are continuing to be improved, as well as looking at new processing methods.

In the latter category, we can discuss the use of atomic energy in food preservation or, more specifically, the use of ionizing radiations

to sterilize and preserve foods, which involves treating the foods after appropriate packaging with atomic rays and then permitting the food to be stored prior to use without the use of heat.

There is only a small temperature rise during the course of the processing procedure. In any food preservation technique it is essential to look at the quality attributes of a food and determine the influence of such a processing method on those attributes. This would relate primarily to the color, the flavor, the appearance, and cost of the processing methods which require evaluation.

I would like to point out some of the work that is being done on ionizing radiations relative to these quality attributes and to indicate some of the potential future applications that may arise from this very interesting potential application of atomic energy.

Representative PRICE. Could you first describe to us the makeup of the American Meat Institute Foundation, how extensively it, as an organization, is in this program and what its connections are with the Atomic Energy Commission program?

Dr. SCHWEIGERT. I would be very happy to, sir.

The American Meat Institute Foundation is a not-for-profit research and educational institution affiliated with the University of Chicago. We are supported by voluntary contributions from the meatpacking industry and also do research by support from grants and contracts outside of the meat industry similar to other public institutions.

In this particular development, we initially became active in it by virtue of the interest and support of a contract from the Atomic Energy Commission about 5 years ago, who were interested in possible utilization of gross fission products for peacetime use, one possibility being food preservation. This was very early in the development.

In the last 2 years we have been supported in the work on food preservation by the Quartermaster Food and Container Institute of the Armed Forces in their broad contractual program. In addition to the funds that the foundation puts into this work, it is being supported by these Government agencies.

Does that answer your question, sir?

Representative PRICE. Yes.

Dr. SCHWEIGERT. Very good. I wonder if we might have the first slide?

I would like to first orient a bit about the levels of ionizing radiations that are used and how they are measured.

Representative VAN ZANDT. Doctor, are you using reactors? Radiation stems from reactors; is that right?

Dr. SCHWEIGERT. Yes.

Representative VAN ZANDT. Are you using waste material?

Dr. SCHWEIGERT. We are using the spent fuel rods at the Argonne National Laboratory for our radiation source and an experimental cobalt-60 source at the University of Chicago which I will comment on in a moment.

This will give you some indication of the level of dosage required for killing bacteria and other forms of microorganisms which we are interested in. These are usually measured in terms of "rep." The roentgen you may be more familiar with. The "rep" is a unit of ionizing radiation absorbed by food.

This slide (exhibit 40) indicates that the more complex the biological material, the more sensitive it is to radiation.

EXHIBIT 40

Effect of Radiation Dosage on Biological Systems

	Radiation Dosage (rep)
Limit of safety for man	0.3 (per week)
Lethal for man	800
Lethal for insects	25,000
Lethal for vegetative bacteria	50,000-500,000
Food Sterilization (bacterial spores)	1,000,000-4,000,000
Virus, toxin and enzyme inactivation	More than 5,000,000

It takes much less to kill such a complex organism as man than it does to kill the simple microorganisms, which has great implications in terms of providing adequate shielding during the radiation and so forth.

The ultimate objective here is to be sure that all forms of microbial life in food are killed, and for most foods generally in the range of 1 million to 4 million "rep" are sufficient for complete sterilization. Certain foods may require somewhat less, depending on what kind of bacteria are present.

We have a cobalt-60 source, which is shielded in a lead pig, as we call it, and incidentally it is refrigerated, so that we can keep the food sample cold during the radiation, which is very important experimentally. It is located in the Argonne Cancer Hospital at the University of Chicago and is available for our work and others for experimental work on foods.

Representative VAN ZANDT. Is it necessary to have the food frozen or cold?

Dr. SCHWEIGERT. It is not essential. The side effects during the radiation, the undesirable flavor and odor changes, which I will describe in a moment, are minimized if it is radiated in the frozen state or just above freezing. That is the general experience.

Representative VAN ZANDT. Does this apply only to meat?

Dr. SCHWEIGERT. That is the major experience that we have had, yes. This particular source is only an experimental model. It can sterilize a piece of meat about the size of a frankfurter in about 4 hours and can also be used for bacterial cultures.

The next slide (exhibit 41) I would like to summarize these major acceptability factors which we are concerned with. I mentioned previously the color, flavor, the texture, nutrient stability, and the wholesomeness. We have to be very sure that the foods are quite wholesome with any technique of handling process and so forth.

EXHIBIT 41

Factors in acceptability of irradiated foods

1. Color
2. Flavor and Odor
3. Texture
4. Nutrient Stability
5. Wholesomeness
6. Costs

The next slide, please?

I would like to now review some of the chemical changes that occur in foods. Actually, fresh beef is taken and given sufficient radiation to kill all the bacteria. The flavor and odor are quite undesirable and it is very important to find out what the nature of these flavor and odor changes are with the hope that such basic research can provide the clues as to how to circumvent those problems.

Pork products, which we will develop a little later, do not show any particular undesirable effects and there is where one of the greatest opportunities for radiation appears to be, for such products as bacon and pork sausage.

I want to review a little bit of the chemical work underlying some of this work on radiation. Here we are following the dosage (exhibit 42), which you can see over there, from zero to 10 million rep, and the decrease in the amount of a compound we called glutathione in meat. This is a sulfur containing protein constituent in meat and the amount drops as the radiation dosage increases and we get small but significant amounts of hydrogen sulphide formed (H_2S) and this is one of the undesirable chemical constituents in the off-odors that are produced.

EXHIBIT 42

Sulfur Compounds in Irradiated Beef

Dosage 10^6 rep	Glutathione ug./g.	H_2S ug./g.
0	215	0
2	148	.11
4	90	.09
6	73	.08
8	-	.11
10	-	.06

It doesn't seem to be increased greatly as the dosage is increased. However, some recent work in our laboratory shows that it is. That ug/g. refers to micrograms per gram. A more familiar term to you may be parts per million, a tenth to one part per million is present, but yet it is very significant in the effects that it has in terms that it doesn't smell very good to us.

The next slide, please?

There are also certain changes in the fats. While the fats themselves do not cause the off-odors and flavors, they come from the lean of the meat. Nevertheless, it is important to know that the fat stability is good during radiation. This particular slide brings out some values on peroxides.

Actually, that is oxidative chemical change in the fat and it is a laboratory tool of measuring those chemical changes we call peroxide values (exhibit 43). If the packing material permits oxygen to get through, which is true with the Visking casing (it is a film), we see a value there after storage at 5° for 4 weeks of a peroxide value of 18.7.

EXHIBIT 43

Influence of Irradiation and Storage on Peroxide Values of Beef Fat

Dosage 10^6 rep	Irradiated	Stored 4wks. at 5°
	Visking	
0	0.4	0.4
2.1	2.0	18.7
	Saran	
0	0.5	0.6
2.1	1.6	2.6

That food is rancid, which brings out the point that if a Saran casing, which does not let oxygen get through, is used, the value does not go up. It stays about the same, 1.6 to 2.6. This shows that it is vital to irradiate foods where oxygen is kept away, because it accelerates degradative changes if oxygen is present in food.

Representative VAN ZANDT. What kind of material are you using for packaging?

Dr. SCHWEIGERT. These particular examples here are these plastic film types. One can also use a sealed metal can and keep the oxygen out after the radiation.

Representative VAN ZANDT. Does the plastic can keep out bacteria as well as oxygen.

Dr. SCHWEIGERT. Certain plastics keep out both the bacteria and the air or oxygen.

Representative VAN ZANDT. Does the meat remain as it is?

Dr. SCHWEIGERT. There is no change if the oxygen is kept away.

Representative VAN ZANDT. And also the bacteria?

Dr. SCHWEIGERT. That is right. If it is recontaminated it will spoil right away, of course.

The next slide, please (exhibit 44).

EXHIBIT 44

Carbonyls in Irradiated Beef and Fat (Acid-salt Extracted)

Dosage rep x 10^6	Fat moles x 10-5/g	Meat*
0	0.12	3.68
2	0.51	9.49
4	0.86	12.88
6	1.04	15.64
8	1.84	18.17
10	1.55	19.55

* Contained 3.4% fat

This brings out another chemical measurement we have made, what we call carbonyl values in irradiated beef. These are oxidative changes that we thought came primarily from the fat, but when we compared the carbonyl values that we got for irradiated fat or irradiated meat (this is irradiated beef as compared to irradiated beef fat), that actually most of this carbonyl was coming from the lean part of the meat and not so much from the fat.

If the dosage is increased from zero to 10 million rep, there is at least 10 times as much of these carbonyl compounds in the meat as in the fat. That is an important chemical tool to follow the effect of irradiation and you will notice that irradiation dosage increased the amount of these carbonyl compounds in both fat and meat.

We think that these carbonyl compounds may be associated with some of the off-flavors or odors. This is the way we in the chemical laboratory can get a hold of this problem of odor so we have a quantitative measure.

It is very difficult to smell irradiated meat today and 3 weeks from now and decide which one was the worst but if we can get some chemical handles to measure the effect of irradiation we have a way of correlating our experiments.

The next slide (exhibit 45) summarizes the major chemical changes which have been measured in our laboratory as well as in some of the

EXHIBIT 45

Chemical Changes in Irradiated Meat

1. B vitamin destruction
2. Meat pigment alterations
3. Production of peroxides
4. Production of carbonyl compounds
5. Destruction of glutathione
6. Formation of H_2S and CH_3SH
7. Production of fluorescent compounds

other laboratories in the United States. There is some destruction of certain B vitamins; thiamin or vitamin B–1 is destroyed somewhat during irradiation.

Senator BRICKER. To what extent?

Dr. SCHWEIGERT. It is about 70 percent destroyed from the work at the University of California at Davis which is in the upper range of destruction observed during normal heat processing of foods. The other B vitamins seem quite stable to irradiation.

Senator BRICKER. You mean in the cooking process that you will destroy 70 percent?

Dr. SCHWEIGERT. No. There is a 70 percent destruction of thiamin during the irradiation process.

Senator BRICKER. You said by the heat process. In cooking you don't destroy 70 percent of the B–1, do you?

Dr. SCHWEIGERT. You do; yes. That is the high range of the amount of thiamin destroyed. What I was trying to point out is that they are about the same.

Representative PRICE. In other words, if you buy a can of precooked meat today on the market, 70 percent of the vitamin B–1 would be destroyed?

Dr. SCHWEIGERT. That would be the maximum value for standard methods of cooking such as precooked. It could vary anywhere from 20 to 80, but 70 would be the figure I used for radiation.

Representative PRICE. That is the normal conventional manner of precooking meat today?

Dr. SCHWEIGERT. Yes. Thiamin is unstable to cooking, that is to heat.

I didn't mention much about the meat color. I would like to refer to it here. It is like the changes in the production of peroxides and carbonyl compounds. The undesirable color changes are minimized if oxygen is kept away from the meat. If it is irradiated in a sealed can, as Mr. Van Zandt asked about, or in a plastic bag which keeps oxygen out, the color of irradiated meat is really very good and it stays quite good during storage as far as we have gone.

I have mentioned the destruction of glutathione, the sulfur-containing protein constituent. At the same time H_2S (refers to hydrogen sulfide) and CH_3SH (methyl mercaptan) is formed. These are very undesirable compounds because they are very odoriferous. The people at Oregon State have detected what we call fluorescent compounds. These are compounds which show certain characteristic light absorption phenomena and this characteristic is just a way of following them in the laboratory.

On an overall basis, what I am interested in bringing out here is that rather than just irradiating foods, smelling them, tasting them, looking at them, we are now getting some chemical basis for following the effects of radiation which puts it on a much sounder basis to make intelligent judgments in future research, as well as potential acceptability characteristics.

Bear in mind that pork products such as bacon and pork tenderloin and pork sausage show very little undesirable change compared to beef. We think this is a real approach to ask ourselves why is pork different from beef and it might give us some clues as to how to improve the acceptability of beef.

So that we are thinking now not so much in terms of will radiation be used for all foods, but what about those that show particular promise; those that seem to offer some real opportunities.

Representative VAN ZANDT. Am I correct in stating that in handling the pork, you kill trichinosis, and in addition you preserve everything else?

Dr. SCHWEIGERT. Yes, with these irradiation doses, the trichinosis organism is completely killed, so that it is an added attribute of this process.

Senator BRICKER. They are killed in cooking; aren't they?

Dr. SCHWEIGERT. Yes, sir, in the normal cooking procedure they are.

Representative VAN ZANDT. What about the effect of freezing and thawing of pork? Does that make any difference?

Dr. SCHWEIGERT. It is not clear to me in what connection?

Representative VAN ZANDT. For example, you irradiate a piece of meat and then you freeze it; then, when it is exposed to heat and thaws, what about the trichinosis?

Dr. SCHWEIGERT. The trichini, once killed, so far as we know, would not be influenced by temperature changes.

Representative VAN ZANDT. Trichinosis is then permanently killed.

Dr. SCHWEIGERT. Yes, sir.

Representative VAN ZANDT. Concerning beef that is packaged either in a plastic bag or a tin can, what is the time factor as far as its use is concerned?

Dr. SCHWEIGERT. That is a question that hasn't been thoroughly explored. We have had some beef that has been in a sealed can, sterilized, and kept at room temperature for a period of 6 months, opened the meat up and prepared it and tasted it. It has about the same degree of undesirable odor or flavor as it had right after radiation.

Some of the tests show that it is better after a period of storage than it was right after radiation. The difficulty is defining what do you mean by "right after radiation." We get it back from Argonne National Laboratories several hours after it is radiated actually, while someone else could be testing it sooner.

Representative VAN ZANDT. When the beef is sterilized in the can and then removed from the can, what period of time would the housewife have to cook it before it spoils?

Dr. SCHWEIGERT. As far as we are concerned, it would be preferable to cook it soon after opening the can. In other words, go right ahead with it. We have some indications not well documented yet scientifically that once it is reexposed to air again there is some further undesirable changes that occur more rapidly than with nonradiated meat after it is opened.

Representative VAN ZANDT. In the packaging of beef where the plastic bag is used, does the drip from the meat, caused by moisture that is formed in the inside, affect the meat in any way?

Dr. SCHWEIGERT. There is some additional drip after radiation. It does not seem to be a serious problem. One suggestion that has been given is that an absorbent backing could be put in the package to take up that drip that is formed.

More drip, I feel quite sure, would form from alternate freezing and thawing. That is a very undesirable way to handle meat as far as drip loss is concerned. Actually, the nutrient value is not affected other than what you would lose in the drip, which is very minor.

I would like to now turn attention to lower levels of radiation, not those that require killing all the bacteria, but what about the applications where a major portion of the bacteria are killed and where we are interested in extending the shelf life of a product without providing complete killing of all the organisms. I am sure you are familiar with the low-level applications and the delaying of sprouting of potatoes and deinfestation of grain, and I won't touch on those here.

I would like to indicate some of the potentialities with extending the shelf life of prepackaged meat kept under refrigeration. This slide shows that fresh meat such as fresh beef prepackaged could be irradiated with a level of radiation of about 75,000 rep, which does not kill all the bacteria, but will kill sufficient numbers so that the shelf life under refrigeration can be extended up to fivefold.

This could be very important, we think. One reason this is of interest is that it is such a low level you don't have significant undesirable flavor and odor development, so that problem is not with us when we use low levels of radiation.

In cured meats such as luncheon meats and so forth (exhibit 46), there are different types of micro-organisms present then in fresh meat and it takes a higher dosage to get a significant reduction in the number of bacteria and in that case about 200,000 rep could give a twofold increase in the shelf life of meat under refrigeration.

EXHIBIT 46

Extension of Shelf Life by

Ionizing Radiations

Fresh Meats (75,000 rep)
up to 5-fold

Cured Meats (200,000 rep)
up to 2-fold

We would like to emphasize that this is shown experimentally and we know that when those go out into actual practice there may be factors that we are not aware of that could alter the optimism for this, but we believe it is of sufficient promise to merit close scrutiny.

Representative VAN ZANDT. In exposing the cured meat at 200,000 reps, could you give us the time factor involved? What is the time of exposure?

Dr. SCHWEIGERT. The time factor would, of course, vary with the radiation source. With the one we are using at Argonne National Laboratory, this would be on the general order of 10 minutes with the spent fuel rod source we have there.

With some of the manmade beta ray machines, we give somewhat more limited penetration than these gamma sources; they can give that sort of dosage in a matter of seconds with those machines.

Representative VAN ZANDT. Considering the higher number of reps, and a sizable piece of beef, what would the time factor be?

Dr. SCHWEIGERT. The biggest pieces of meat that we have facilities to irradiate are about equivalent to a No. 10 can. That could be done at Material Testing Reactor at Idaho. The most potent fuel rods that we have had for the experiments we have worked with would take about a half hour to give sterilization. At certain times it will take an hour or 2 hours, depending on how active the spent fuel rod sources are, but that is quite adequate for the experimental work.

Representative VAN ZANDT. Then the time factor depends on the strength of the gamma ray that is contained in the beam?

Dr. SCHWEIGERT. That is correct. The next slide, please?

This slide (exhibit 47) gives another approach which our bacteriologists have been working on, and that is what are the possibilities of irradiation in connection with antibiotic treatments for extending the shelf life of meats.

EXHIBIT 47

Microorganisms Limiting Life of Fresh Meats

1. Untreated: Pseudomonads
2. Irradiated: Microbacteria
3. Antibiotics: Pseudomonads
4. (2 + 3): Yeast and Molds

To date neither radition nor antibiotics has been approved as a procedure by the Food and Drug Administration for red meats, but we are interested in them experimentally. This points out that fresh meat keep under refrigeration will spoil as indicated when no treatment is given, because of organisms called pseudomonads.

No. 2, irradiated, the first organisms that spoil the meat are called microbacteria, which tells you that the pseudomonads are killed, but another groups comes up and spoils the meat. When antibiotics alone are used, the pseudomonads spoil the meat because the antibiotics are not particularly effective againsts the pseudomonads, but the beauty of it is that if antibiotics and radiation are used together, they are more effective than either one alone.

In that case both the microbacteria and the pseudomonads are inhibited and ultimately the meat will be spoiled by yeasts and molds. The significance here, I think, is that irradiation in combination with other preservation techniques should not be lost sight of and maybe in combination with other treatments such as antibiotics, they will be even more promising than when used alone.

Representative VAN ZANDT. Doctor, I have a question regarding that particular chart. Do you use the radiation and the antibiotics at the same time?

Dr. SCHWEIGERT. In the treatment No. 4, we actually put the antibiotic on the meat and then irradiate it. This is a low-level treatment of about 75,000 reps.

Representative VAN ZANDT. How do you apply the antibiotics?

Dr. SCHWEIGERT. In this particular case, they were small pieces of meat that were dipped in an antibiotic solution.

Representative VAN ZANDT. Are they irradiated?

Dr. SCHWEIGERT. Yes.

Senator BRICKER. There is usually a process by which they treat the carcass just as you embalm one by shooting the antibiotic into the blood stream right after the killing?

Dr. SCHWEIGERT. That is correct.

Senator BRICKER. What effect would the feeding of antibiotics during the growth period have upon the meat? The same thing as if it were shot in at the time they were destroyed?

Dr. SCHWEIGERT. The levels of antibiotics that are now used in feeding would not result in any significant amount of the antibiotic in the tissue.

Senator BRICKER. Remaining in the tissue?

Dr. SCHWEIGERT. That is right. There would be insignificant amounts in the tissue, so that the way to get a significant——

Senator BRICKER. Like the effect you get from a feeding?

Dr. SCHWEIGERT. That is right. A few overall things perhaps might help summarize it.

Representative VAN ZANDT. I have another question, Doctor. Have you been able to develop a definite cost factor?

Dr. SCHWEIGERT. We ourselves have not worked with it. Other people who have, give a prediction of somewhere from 1 to 7 cents a pound. There, again, the Quartermaster——

Representative VAN ZANDT. From 1 to 7 cents a pound?

Dr. SCHWEIGERT. Right. This, of course, would be of greater economic feasibility with a high demand food such as meat than with a food of lower value per pound to absorb the processing cost. There certainly will be no application of this procedure until the Food and Drug Administration has had an opportunity to evaluate the extensive experiments being done on the wholesomeness of these products.

So far this looks most encouraging. In addition, we think that we are not going to have mass changeover, even if the Food and Drug Administration approves it, and even if the costs are feasible, because certain food shows significant undesirable effects.

It is a real challenge to attempt to circumvent these off-flavor and odor problems with certain of the beef products particularly.

Senator BRICKER. What is the other compound in addition to H_2S?

Dr. SCHWEIGERT. Methylmercaptan. We do not mean to infer that there aren't additional ones.

Senator BRICKER. Those two you detect?

Dr. SCHWEIGERT. Yes, sir; we can identify and measure.

Representative PRICE. How encouraging are the prospects of getting this meat back to favorable taste?

Dr. SCHWEIGERT. For instance, with beef I would say that the problem is quite difficult, and we think it can be solved or we would be foolish to be working on it, but you can't give a prediction when you know it is a very tough problem. It is not right around the corner, because it is very tough chemistry and when you consider the number of alternatives that would be acceptable to the Food and Drug, even if you knew what the mechanism was, it is not overly optimistic, I would say. It will take some time to solve.

Representative PRICE. One has to test it otherwise?

Dr. SCHWEIGERT. If you are interested in its application for all foods; yes, sir.

Representative VAN ZANDT. Doctor, have you found any toxicity in the meat?

Dr. SCHWEIGERT. We ourselves have not been measuring it but the other laboratories in the United States have, but found nothing deleterious to the growth and reproduction of animals insofar as those tests have gone. They have used the rat, chick, and monkey.

Representative VAN ZANDT. What is the difference between meat in its natural form and ground hamburger? Is there any difference?

Dr. SCHWEIGERT. It is a very good question. In what connection?

Representative VAN ZANDT. Let us assume you have a quarter of beef from which you cut meat and convert it to ground hamburger. Is there any difference in the result you get from irradiation?

Dr. SCHWEIGERT. You are speaking with respect to radiation treatment?

Representative VAN ZANDT. Yes.

Dr. SCHWEIGERT. They are from our experience essentially the same. In other words, if you are wondering whether the acceptability, the off-flavor or odor, is significantly different, I believe we would have to say they are not, but these are very difficult to be absolutely exact about because the ability to detect differences in off-flavors and odors is quite hard, but they are not grossly different.

Representative PRICE. In that connection, Doctor, I would say that we had testimony earlier in the year from the Army on the new experiments that were held at Fitzsimons Hospital last year. Tastes were the only unsatisfactory condition of those tests but no other points were raised.

We are going to put that section of the hearing that we have already held in with these hearings.

Dr. SCHWEIGERT. I think the real opportunity lies in looking at least at most of those products that are very good for radiation, to get the experience of irradiation the application in the industries and in the meantime, more and more of these foods which at the moment appear to be less desirable in the sense of flavor and odor can be worked on and we hope circumvented one by one.

I think another approach to the problem perhaps is to look a little bit more on the potentialities of a new market for radiated foods. We get in the habit of comparing them with what we have all the time and there may well be places where we are not doing a good job with foods in a distribution way, where irradiated foods can be of potentially great value, not only to the military, but to the civilian economy.

This could conceivably be in other countries that do not have good preservation facilities at the present time, as well as in this country. We also believe it is important for various companies, particularly in the food business, to follow these developments and to know what is going on in the field of radiation because it takes a certain amount of know-how, and if and when some of these applications which we believe will be forthcoming in a few years actually occur, they will be in a position to make some real sound business judgments and we certainly need that sort of technical know-how in the food industries to be right on the forefront of utilization of agricultural products as much or more than anywhere else that I know of.

Thank you very much.

Representative PRICE. Thank you, Doctor. I certainly hope that you whip the taste factor, because I know what the Army is starting out with.

Senator BRICKER. You have to prevent the change in the meat in the first place. You never reestablish it after it once has been affected?

Dr. SCHWEIGERT. It is possible we could solve it after they were formed by some simple way of removing it. The most optimistic approach is to prevent them from happening, as you have pointed out; that is right.

Representative VAN ZANDT. Believe me, some of the meat I tasted while in military service was in need of change.

Senator BRICKER. Of course, as to your suggestion there that you might establish this irradiated meat as value in some places, it would not be any worse so far as the odor and taste is concerned than some of the cheese they eat.

Dr. SCHWEIGERT. I don't think we should underestimate the opportunity for a home economist to develop the taste. We have had a few people taste these products that rather liked the flavor. It is new. It is so easy to get in the habit. It doesn't taste like what you are used to and, therefore, you don't like it

Representative PRICE. Is it a flat taste?

Dr. SCHWEIGERT. This is a highly individualistic answer. I personally don't have too much objection to it as compared to some of the young girls in my research group, but it is rather slightly bitter. It is a somewhat bitter and sulfurous taste. It isn't particularly desirable, I can assure you.

Senator BRICKER. If we never tasted good meat it might be all right?

Dr. SCHWEIGERT. Some people think meat as prepared by some people is most undesirable and maybe they will like this. It is a highly individualistic thing.

Representative PRICE. How are the facilities that you are working with, Doctor? Are you adequately set up? Are you working under handicaps or obstacles that you would like to see removed?

Dr. SCHWEIGERT. No. I think we are quite pleased with the facilities provided through the Atomic Energy Commission at Argonne, and with the Quartermaster's broad program, and support.

The facility of the cobalt–60 source at the university is most helpful to us, which is another atomic-energy installation. I feel very good about the program and we believe that we have learned a lot in 5 years, and we have a lot more to learn in this field. It is a very important one.

Representative VAN ZANDT. Doctor, it was suggested during the past several months that possibly the Government should subsidize the construction of research reactors on the campus of these colleges and universities throughout the United States.

In this instance, would it not be very helpful to you to have a research reactor on the campus of the University of Chicago?

Dr. SCHWEIGERT. That is correct.

Representative VAN ZANDT. Have you ever requested such a facility?

Dr. SCHWEIGERT. No; we have not.

Representative PRICE. Have you ever thought about it?

Dr. SCHWEIGERT. Yes; we have, and we are very interested in the potential application of a food-processing unit with a reactor setup.

I understand there is some interest in having one or more built in this country, which we would be most interested to see.

Representative PRICE. You do not now have exclusive use of any one reactor; is that right?

Dr. SCHWEIGERT. No; we do not.

Representative PRICE. It would help in your work, wouldn't it?

Dr. SCHWEIGERT. There would be occasions when it would, although the scheduling for the fuel rod assemblies at Argonne has worked out quite well, everything considered. It is a give-and-take proposition.

Representative PRICE. You have never been delayed in your program waiting for facilities you used?

Dr. SCHWEIGERT. Not unduly, I wouldn't say. There are some times when we have to wait a day or two to get the use of it.

Representative VAN ZANDT. Doctor, are you receiving many inquiries from the nationally known packers, processors, and food handlers?

Dr. SCHWEIGERT. We are receiving a tremendous number. In fact, a number of their research people have come in to see us at various times and one of the first questions they have asked us, where they do not have a research group on radiation, is what is the possibility? Should we be in the field?

The minimum we tell them is that they should be following it very closely, because this is a very vital opportunity for the progressive food person if and when this thing breaks.

Representative VAN ZANDT. In your field, you have made a study of poultry?

Dr. SCHWEIGERT. We have not worked with poultry at all at our place. We understand from other work that it looks quite good.

Representative VAN ZANDT. You displayed a chart that concerned the single body dose than man could take. Would you please put that chart on the screen again?

Dr. SCHWEIGERT. That is No. 1. This was a generalization showing that a single body dose of approximately 800 roentgens would be lethal to man as compared to 1 to 4 million to kill many of these simple microorganisms.

Representative VAN ZANDT. Of course, you do not infer that any of this dosage is left in the meat offered for human consumption.

Dr. SCHWEIGERT. Absolutely none in the meat; no.

Senator BRICKER. One more question. There is no effect as far as taste and odor is concerned in the use of the antibiotics, is there?

Dr. SCHWEIGERT. Not so far as our experiments have gone. There is absolutely no difference. It is a tool for controlling the spoilage.

Representative VAN ZANDT. Does the antibiotic in any way act as a film that would resist the gamma ray or the electrons?

Dr. SCHWEIGERT. No. The antibiotic would in no way affect the penetration by gamma rays.

Representative PRICE. Thank you very much, Doctor.

Dr. Dunham, would you proceed?

Dr. DUNHAM. Mr. Price, the next scientist we bring to report to you is Dr. Samuel Brody, professor of dairy husbandry and leader of climatic project, College of Agriculture, University of Missouri.

Dr. Brody is going to talk about the use of radioisotopes in the study of milk and beef production under different climatic conditions.

Representative PRICE. Dr. Brody?

STATEMENT OF DR. SAMUEL BRODY, DEPARTMENT OF DAIRY HUSBANDRY, UNIVERSITY OF MISSOURI, COLUMBIA, MO.

Dr. BRODY. I think I can tell my story best with the aid of a series of slides.

The first slide (exhibit 48) shows three categories of our experimental cows: Holstein, Jersey, and Zebu (Brahman) exposed to a barn temperature of 100° F. The Holstein cow appears to be very distressed. The Jersey is somewhat less so. The Zebu cow is not distressed at all.

Temperature (climate, weather) is thus seen to be an important stressing factor. While we can control many other factors in animal production, we cannot control climate on a large scale. We are therefore trying to study the effects of climate on cattle in the hope of ultimately developing productive cattle that would be heat-tolerant, especially needed in our hot humid States and in the tropical regions of the world where highly productive cattle do not thrive, and where milk is scarce and urgently needed.

While European-evolved cattle do not tolerate 100° F. temperatures, Indian-evolved cattle (Zebu or Brahman) seem to be very tolerant to 100° F. The reason for the Zebu heat-tolerance is that they evolved a number of heat-dissipating devices. Some of these devices are visible and others are not visible. I shall discuss both presently.

The Holstein is rather less heat-tolerant than the Jersey because the Holstein is a larger animal, and the larger the size of a body the smaller its outer surface (per unit of weight) for heat dissipation.

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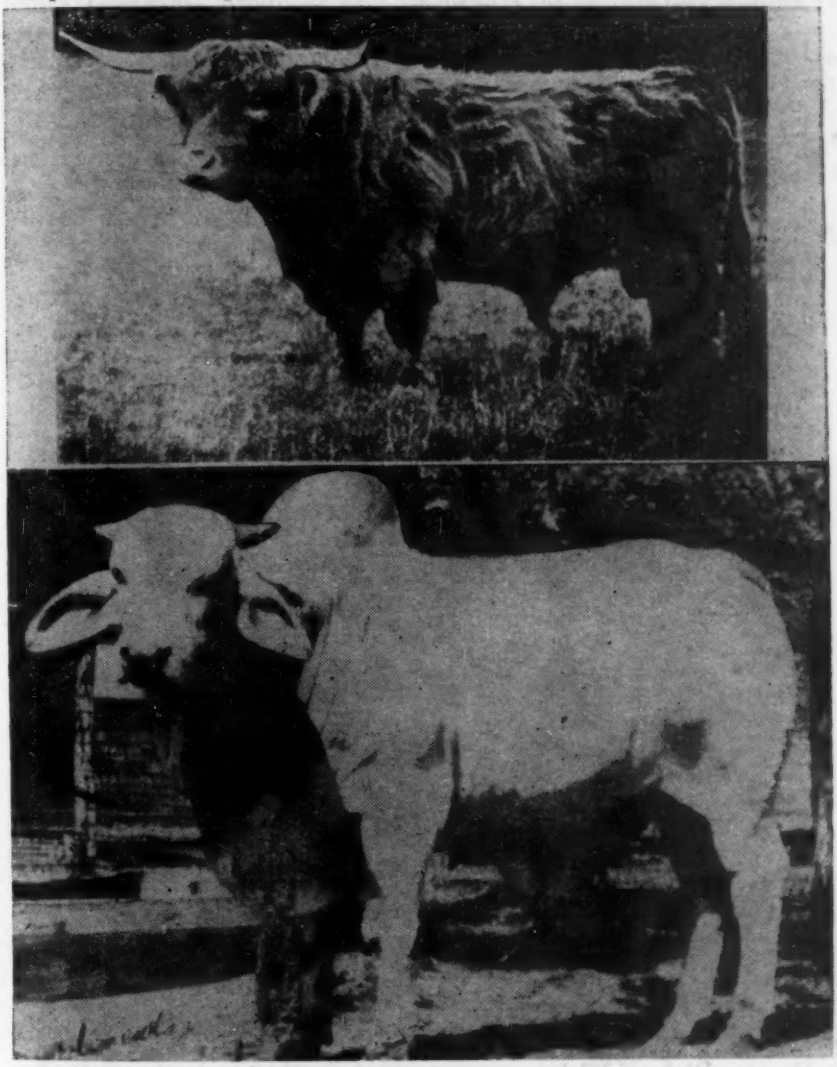
EXHIBIT 48. Three categories of experimental cows: Holstein, Jersey, and Zebu (Brahman) exposed to a barn temperature of 100° F. The Holstein cow appears to be very distressed. The Jersey is somewhat less so. The Zebu cow is not distressed at all.

The second slide (exhibit 49) is another example of two animals having widely different heat-dissipating mechanisms. One is a Zebu bull of large dewlap, ears, and sheath, all of which act as heat dissipaters; and short, stiff hair, which do not interfere with heat dissipation.

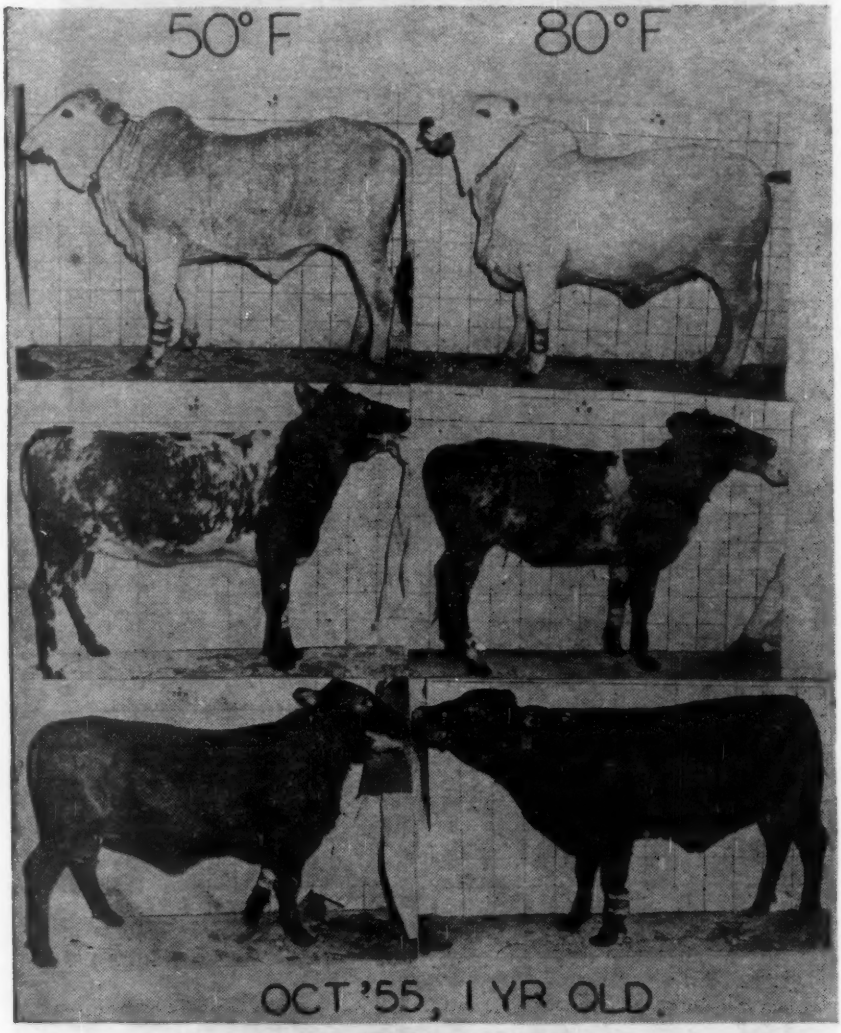
EXHIBIT. 49. Comparison of the appearance of cool-climate (compact, heavy fur) and tropical-climate (loose build, loose skin folds, short hair) cattle—an example of visible adaptation.



The reserve fat in the Zebu tends to be deposited in the hump rather than under the skin as in European cattle where it would interfere with heat dissipation. The other bull is from Scotland, a country with a raw climate. The European-evolved bull had long, fleecy hair, compact body build, and subcutaneous fat for conserving instead of dissipating heat as in tropical cattle.

We experimented in our climactic laboratory with various categories of animals and we show in this third slide (exhibit 50) three categories of heifers: Shorthorn, a cool-climate British breed; Zebu, a tropical breed adapted to hot climate; and a new breed, the Santa Gertrudis.

EXHIBIT 50. Relative growth made in about a year by the three categories of heifers—Zebu, Shorthorn, and Santa Gertrudis. The Shorthorn housed at 80° F., with severely depressed thyroid activity, weighed at 1 year of age about 200 pounds less than the Shorthorn housed at 50° F., or the Zebu or Santa Gertrudis housed at either 50° F. or 80° F.



Senator Richard Kleberg—maybe Senator Bricker remembers him—and his brother, Robert Kleberg, Jr., crossed the Zebu with the Shorthorn and, by appropriate selection and matings in successive generations, developed this new breed of cattle, the Santa Gertrudis cattle, which combine the heat- and insect-tolerance qualities of the Indian

Brahman or Zebu) with the beef-producing qualities of the European (Shorthorn) cattle.

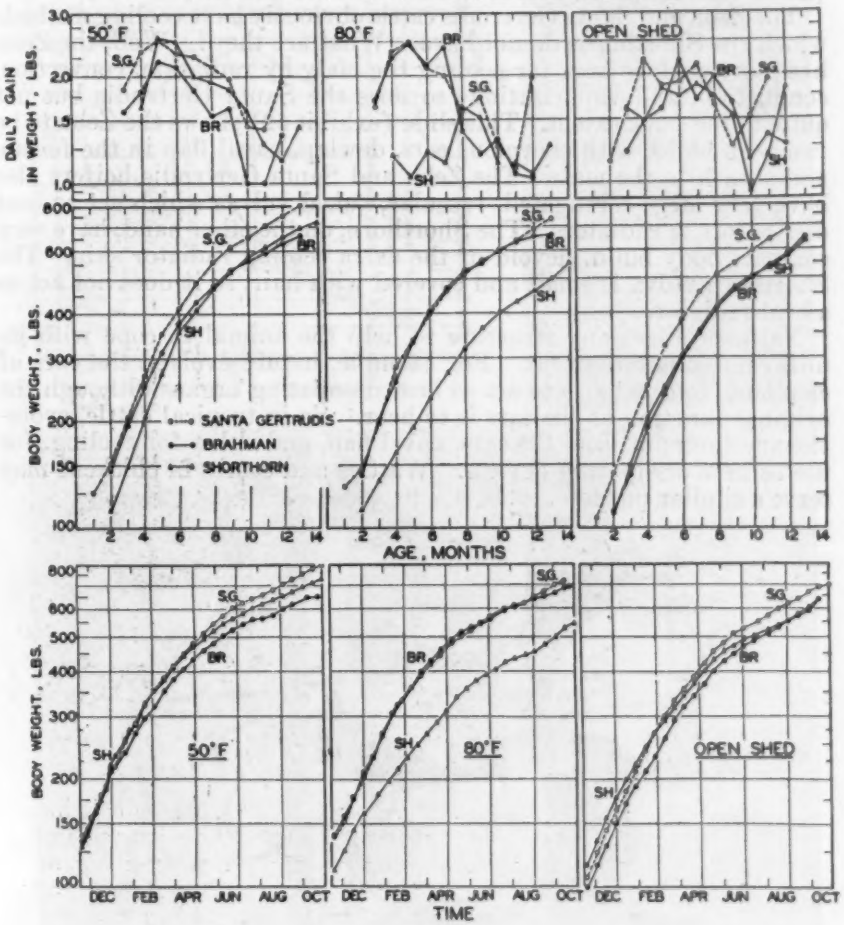
Representative VAN ZANDT. Do you mean Dick Kleberg, of Texas?

Dr. BRODY. Yes. Dick Kleberg and his brother, Bob Kleberg, who is the president and manager of the King Ranch.

The Zebu did not produce the desired kind of beef. The Shorthorns did produce the desired kind of beef in cool climates but not in Texas; they could not stand the south Texas climate, nor the Texas tick. The Santa Gertrudis produces excellent beef and is heat- and insect-tolerant.

The fourth slide (exhibit 51) shows differences in effect of climate on these three different breeds of cattle. One group of heifers of each breed was subjected to a temperature of 80° F.; another to 50° F. Notice the difference. The Zebu heifers grew as well at 80° F. as at 50° F. The Shorthorns, on the other hand, were stunted by the 80° F. temperature, they weighed 200 pounds less than those at 50° F.

EXHIBIT 51. Age curves of growth in weight and in gain in weight at 50° F. (left), 80° F. (center), and open shed (right).



In brief, Shorthorn cattle are not heat-tolerant, whereas Zebus are heat-tolerant.

As I said, the Klebergs crossed the heat-tolerant Zebu with the non-heat-tolerant but highly productive Shorthorns, and by appropriate selections in successive generations evolved the Santa Gertrudis breed of cattle. The Santa Gertrudis cattle, shown in this slide, combine the best qualities of both breeds, the heat tolerance of the Zebu and the high beef-producing qualities of the Shorthorns.

The Klebergs were good enough to let us investigate their Santa Gertrudis cattle. I brought a dozen of their heifers to our laboratory, and compared their rate of growth with those of their parent stock, that is, Zebus and Shorthorns. We kept them all under the same conditions, except that one group was kept at 50° F. and the other at 80° F.

As I said, at 80° F. the Zebu grew as rapidly as at 50° F. The Santa Gertrudis grew equally well at 80° F. and 50° F. but the Shorthorns were stunted by the 80° F. temperature. In other words, the Santa Gertrudis inherited the desirable evolutionary resources—heat tolerance of the Zebu and beefiness of the Shorthorns—of both breeds (Zebus and Shorthorns).

The Zebu and Santa Gertrudis cattle obviously have cooling methods which the Shorthorns do not have. What are they? Well, the Zebu has more surface area for cooling the body by radiation, convection, conduction, and vaporization; so does the Santa Gertrudis but not quite to the same extent. This slide (exhibit 52) shows the Zebu to be rangy in build, with enormous ears, dewlap, naval flap in the female and sheath in the male. The Zebu and Santa Gertrudis heifers also have very large corrugated, vascular, naked vulvas which act as heat dissipators or radiators. The Shorthorn, on the other hand, have very compact body build, devoid of the extra cooling radiator skin. The Shorthorn vulva is small and covered with hair, so it does not act as a heat rediator.

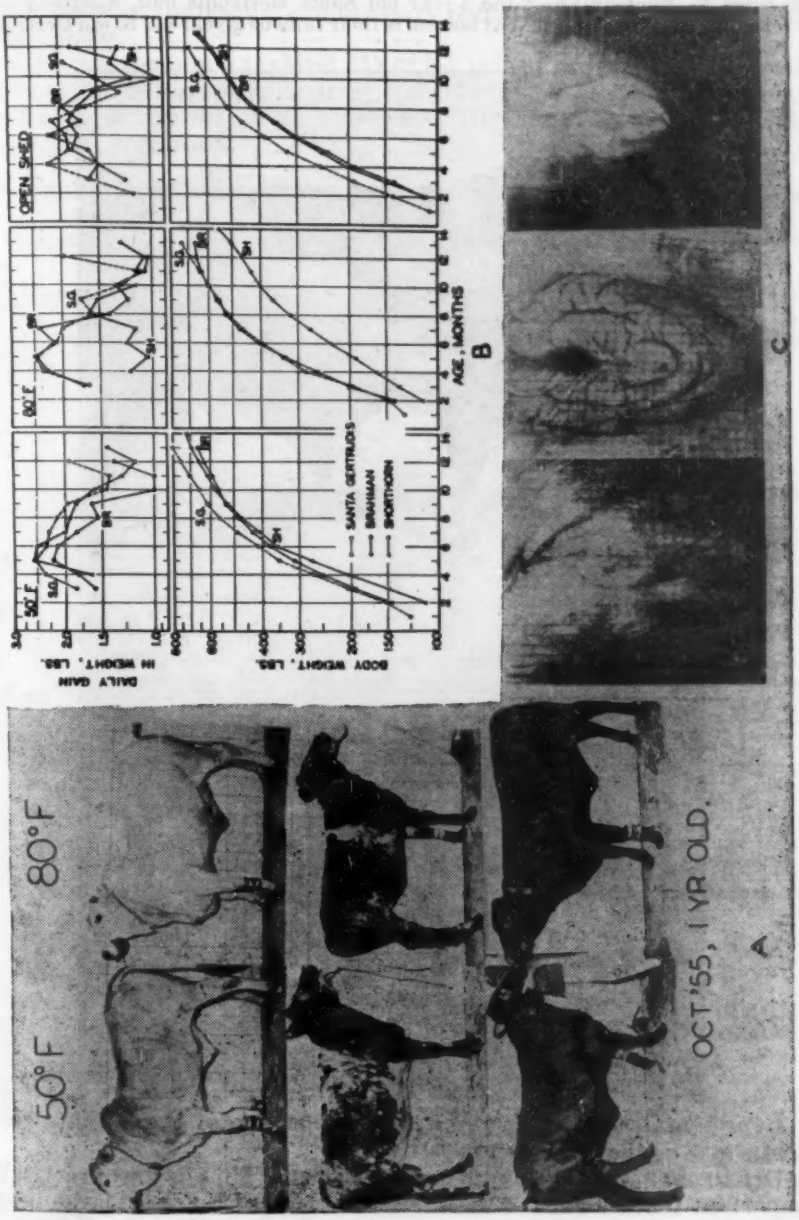
Nature utilizes any structure to help the animal to cope with its unfavorable environment. For example, nature evolved the ears of elephants to great size to act as heat dissipating organs although the original function of the ears is to hear. So in tropical cattle, evolutionary forces utilized the ears, navel flap, and vulva for cooling, for use as heat dissipating devices. Wattles and combs in chickens may serve a similar purpose.

EXHIBIT 52

(a) Photograph of Brahman (top), Shorthorn (middle), and Santa Gertrudis (bottom) heifers. Brahmans at 50° F. had darker hair than at 80° F. The Shorthorns at 80° F. were stunted, but the other breeds did equally well at 50° F. and 80° F.

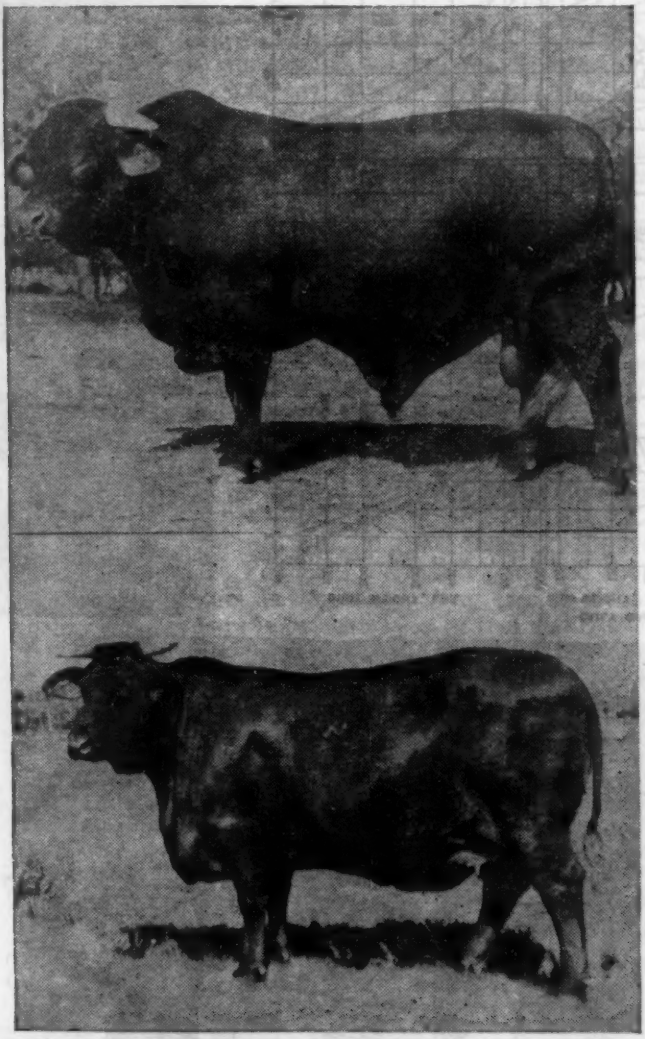
(b) Age curves of growth in weight and gain in weight at 50° F. and 80° F. and open shed.

(c) Relative heat-dissipating surface areas and vascularity of the vulvas of the three categories of heifers at age 1 year.



Here is a recent photograph (exhibit 53) (taken by John K. Cypher, Jr.) of the 3-year-old Santa Gertrudis bull, Kentucky Boy, at the King Ranch; and here is their famous 2-year old Santa Gertrudis heifer, Mama Grande. I do not know whether you are livestock people, but I am sure that you appreciate the anatomic features of these animals that adapt them simultaneously to hot climate and to high beef production.

EXHIBIT 53. Photograph of the 3-year old Santa Gertrudis bull, Kentucky Boy (top) at the King Ranch. At bottom is their famous 2-year old Santa Gertrudis heifer, Mama Grande.



Representative VAN ZANDT. Could either one of these Santa Gertrudis take on the 80° F. temperature?

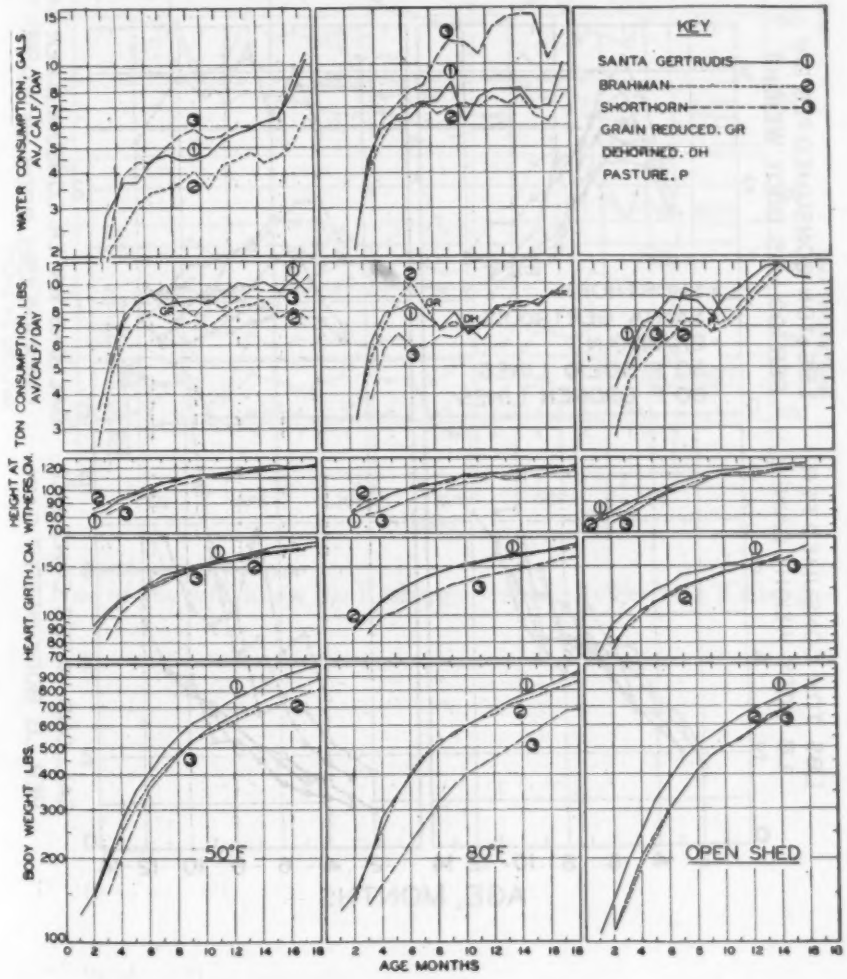
Dr. BRODY. Nearly as well as the Zebus. Thus is the practically important feature about these animals. In spite of their large beefy body they tolerate high temperature nearly as well as the Zebu.

Senator BRICKER. This is the crossbreed type?

Dr. BRODY. Well, it was developed by successive selections from an original cross of a Zebu bull with a grade milking Shorthorn cow. The resulting bull calf "Monkey" was roughly three-eighths Brahman and five-eighths Shorthorn; and "Monkey" is the progenitor of the Santa Gertrudis breed of cattle, at present numbering 85,000 head from which 20 million pounds of beef are marketed yearly. The selections in successive generations were made in such a way as to combine in inheritance of the desired evolutionary potentialities or resources from both breeds.

Here is an example (exhibit 54) of the rate of growth of the animals in the form of curves, comparing the relative growth rates of animals housed at 50° F. with those at 80° F. The other heifers are controls, kept in an open shed.

EXHIBIT 54. Comparison of growth rates of animals housed at 50° F. with those at 80° F. The other heifers are controls, kept in an open shed.



Notice that all 3 categories of heifers grew the same at 50° F., but the Shorthorns at 80° F. weighed 200 pounds less than the other breeds (at 16 months of age).

It is generally believed Zebus are more heat tolerant because they drink more water and they "sweat" more. Our results, shown in the next slides (exhibits 55 and 56) indicate that, on the contrary, Zebus drink less water and "sweat" less than the Shorthorn or the Santa Gertrudis. The Shorthorn drinks most water and "sweats" most. The lower water drinking and lower vaporization by the desert tropical cattle agrees with expectations. Cattle adapted to a desert region with low water supply would be expected to become adapted to low water consumption. In brief, our results contradict the belief that Zebus are more heat tolerant because they sweat more.

EXHIBIT 55. Breed differences in the patterns of cool-water consumption with increasing age. Note that Zebus drink less water than the Shorthorns or Santa Gertrudis.

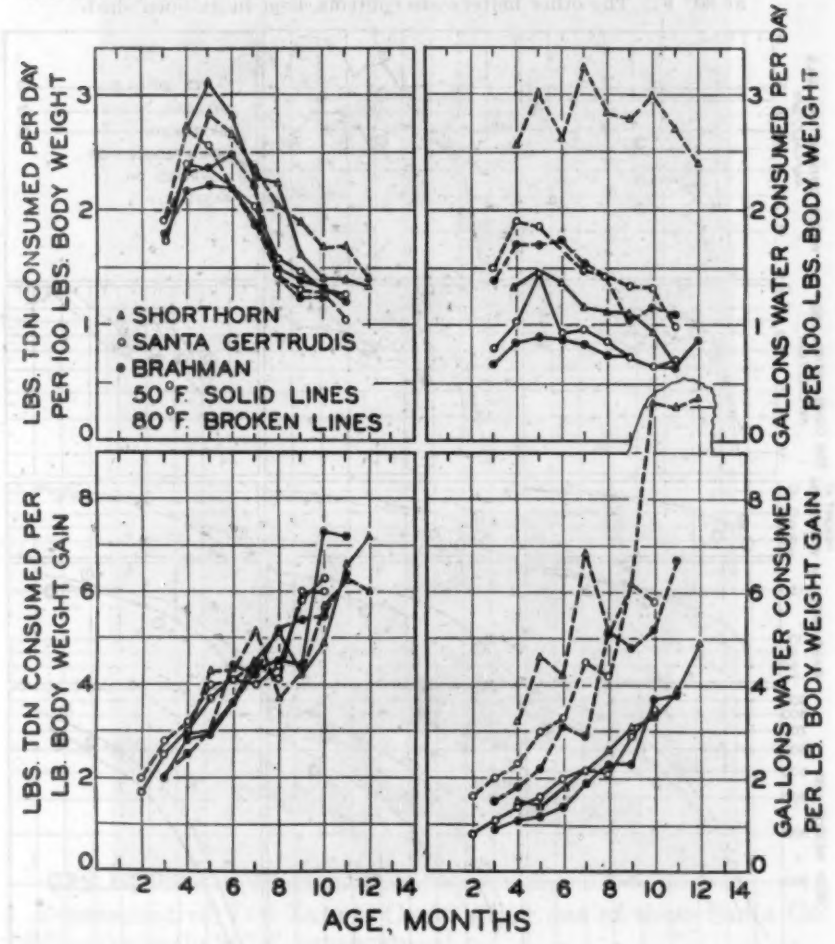
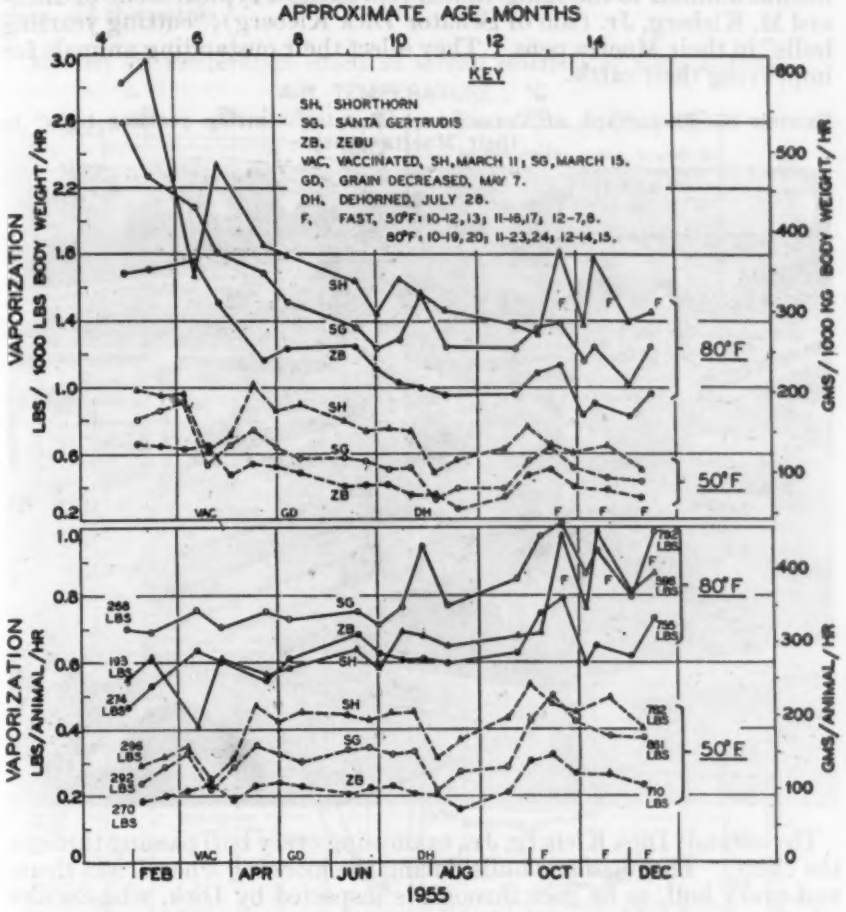

LBS. TDN CONSUMED PER DAY PER 100 LBS. BODY WEIGHT
GALLONS WATER CONSUMED PER DAY PER 100 LBS. BODY WEIGHT
SHORTHORN
SANTA GERTRUDIS
BRAHMAN
50°F. SOLID LINES
80°F. BROKEN LINES
LBS. TDN CONSUMED PER LB. BODY WEIGHT GAIN
GALLONS WATER CONSUMED PER LB. BODY WEIGHT GAIN
AGE, MONTHS

EXHIBIT 56. Comparison of vaporization rates of animals housed at 50° F. with those at 80° F. Note that per unit weight Shorthorns have higher vaporization rates than Zebus.

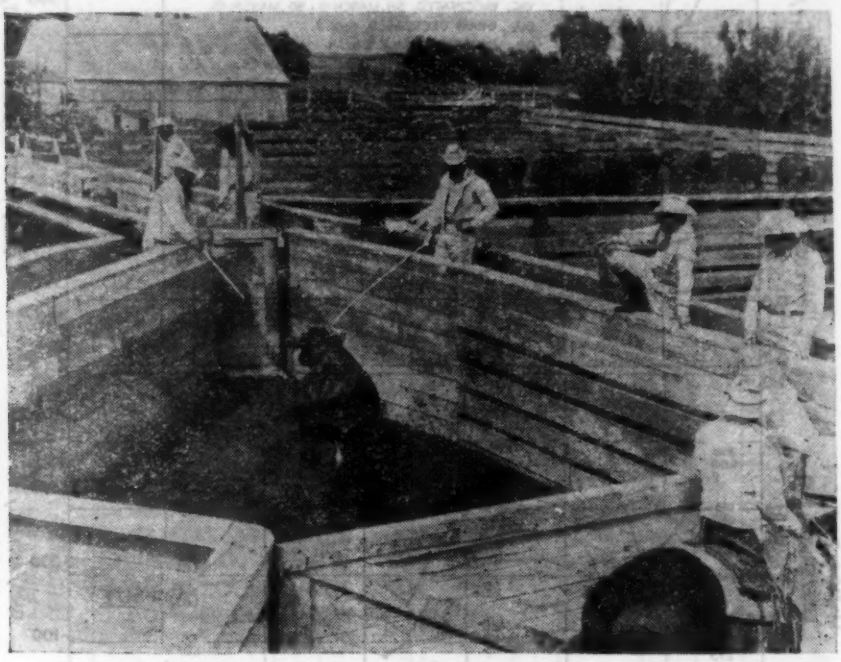


The next slide, please.

Those of you who knew the Klebergs—especially Senator Kleberg—

may be interested to know that this recent picture (exhibit 57) also by Mr. Cypher taken a few weeks ago when I returned the experimental animals to the King Ranch represents a typical scene of Richard M. Kleberg, Jr. (son of Senator Dick Kleberg), "cutting yearling bulls" in their Muerta pens. They select their oustanding animals for improving their cattle.

EXHIBIT 57. Photograph at Texas ranch showing "cutting yearling bulls" in their Muerta pens.

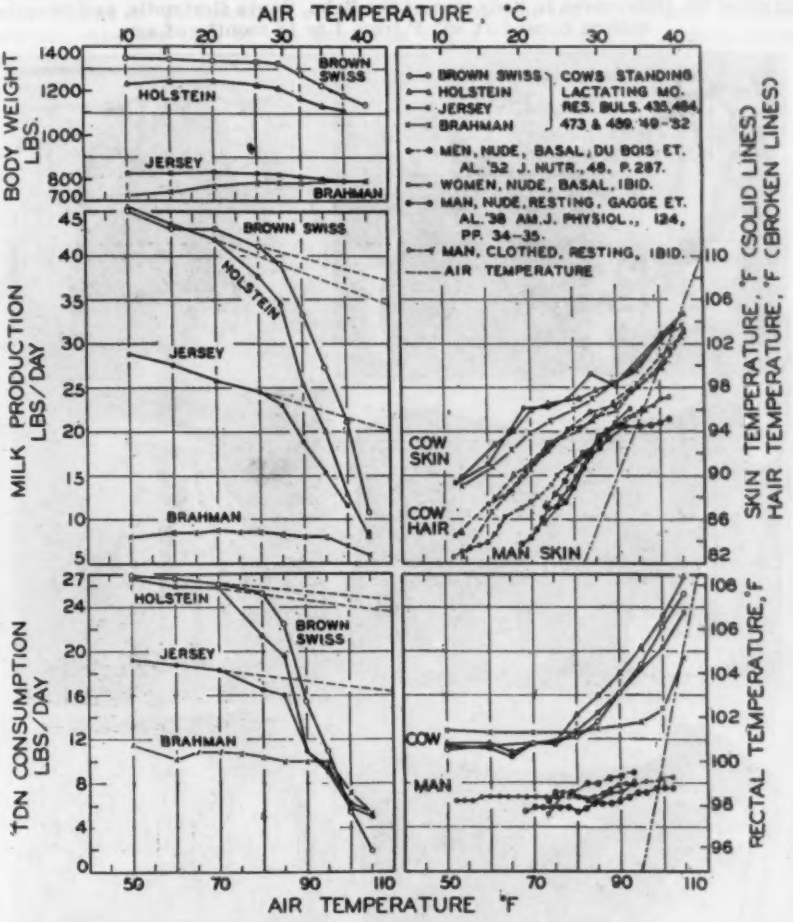


Here stands Dick Kleberg, Jr., examining every bull passing through the chute. They had 300 bulls during the morning when I was there, and every bull, as he goes through is inspected by Dick, who decides whether he should go to the butcher, to the commercial breeder, or to the best breeding herd for further improvement of the Santa Gertrudis cattle.

The Klebergs know cattle, how to select promising breeding stock, and they also have the power—the money, the land, the cattle—with which to develop such a scene of selecting from 300 bulls. An outstanding member of successive generation of the family, personally directs the program of continuous improvement by selection. It is this remarkable combination of power, knowledge, and continuity of policy that makes the King Ranch such a remarkable institution.

The next slide (exhibit 58) shows the way rising room temperature—10°, 20°, 30°, 40°, 50°, 60°, 70°, 80°, 90°, 100°, and 105° F.—affects the rectal temperature—the best index of the thermal condition—of the cattle.

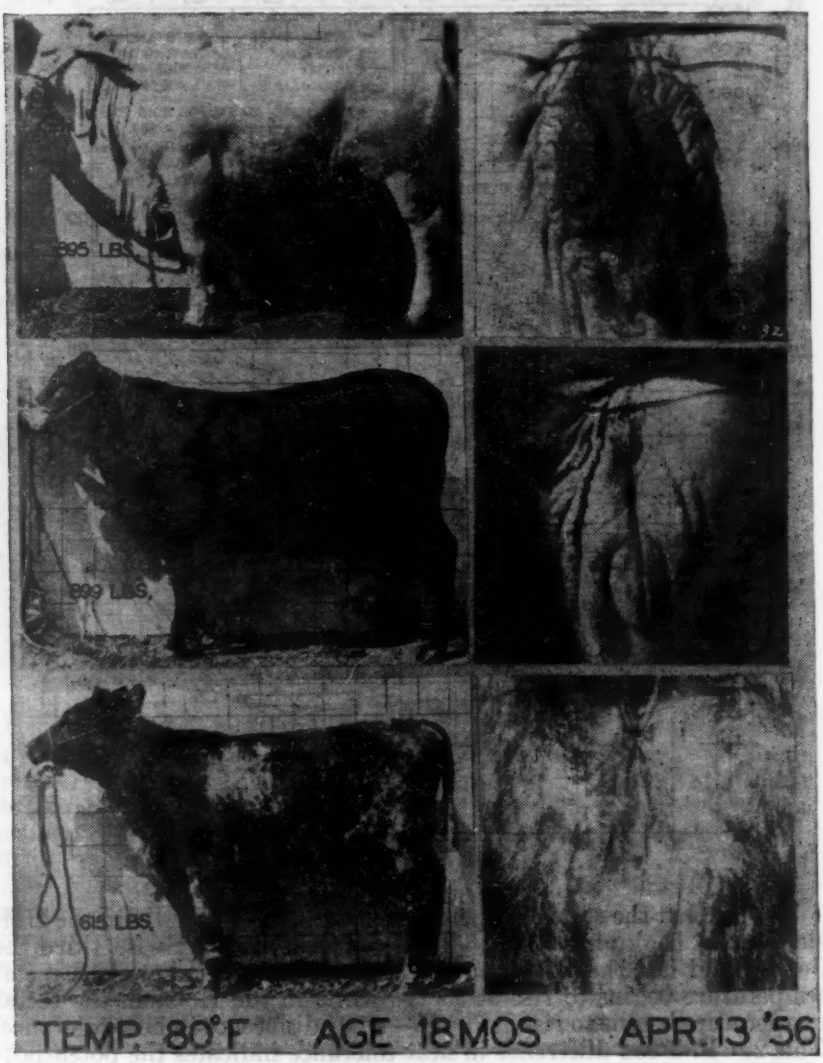
EXHIBIT 58. Temperature effects on several reactions of cattle and man.



You see that the rectal temperature goes up most rapidly in the Holstein cattle, beginning 70° F. Then come the Brown Swiss, third the Jersey, and last the Brahman or Zebu. In the Zebu cows the rectal temperature begins to rise at 95° F, while in the Holstein the rectal temperature begins to rise at 75° F.—a 20° difference in heat tolerance. This 20° F. breed difference in heat tolerance indicates the potentialities for developing heat-tolerant cattle by cross-breeding and selection in successive generations as previously explained.

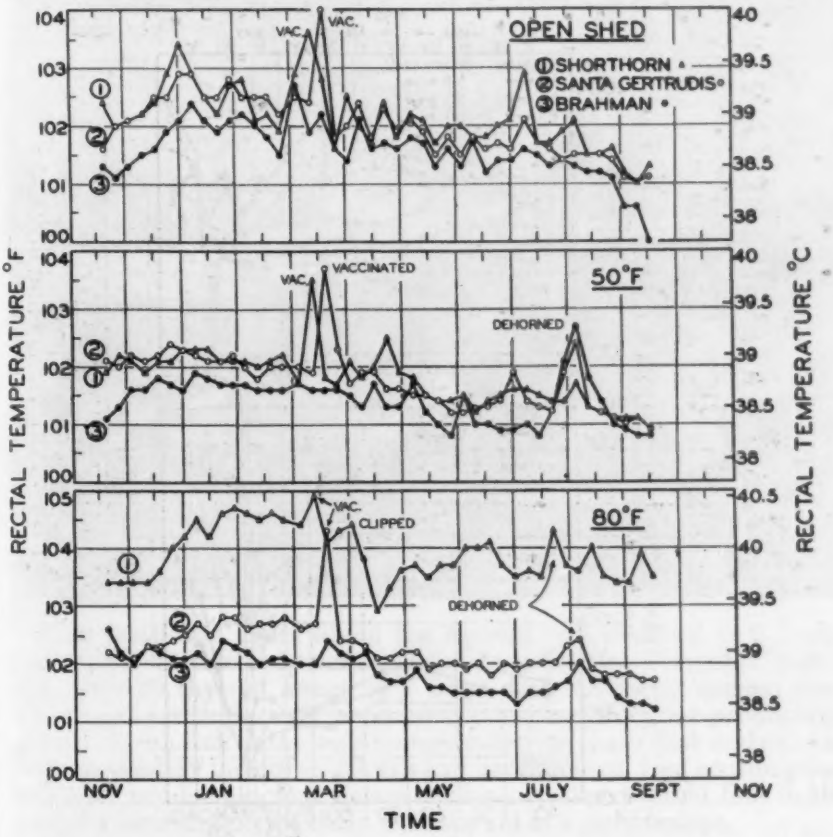
This slide (exhibit 59) shows differences in body size of the Brahman, Santa Gertrudis, and Shorthorn heifers housed at 80° F. from 1 to 18 months of age. The Shorthorn rectal temperature at 80° F. room temperature was 104° F., 2° to 3° F. above normal, whereas that of the Brahman and Santa Gertrudis was normal, only 101° F.

EXHIBIT 59. Differences in body size of the Zebu, Santa Gertrudis, and Shorthorn heifers housed at 80° F from 1 to 18 months of age.



On clipping the Shorthorn's hair, their rectal temperature went down as shown in the next slide, (exhibit 60) but not for very long. The hair promptly grew to the former length and thickness is spite of the heat, as shown in this slide.

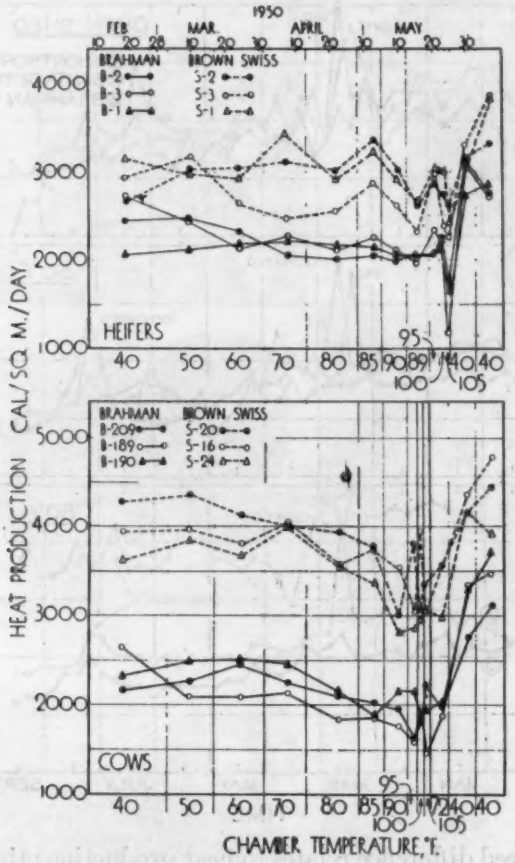
EXHIBIT 60. Curves on rectal temperature of heifers housed at 50° and 80° F. Note that at 80° F. Shorthorn rectal temperature was 104° F., 2° to 3° F. above normal, whereas that of the Zebu and Santa Gertrudis was normal, about 101° F.



Another breed difference relates to heat production; the rate of heat production is much less in the Zebu than in European cattle.

This slide (exhibit 61) shows the relative heat production in milking cows (Zebu and Swiss) and also of Zebu and Swiss heifers—heat production is much higher in the Swiss (European) than in the Zebu (Indian) cattle. The situation is somewhat analogous to that of man—European man has a higher heat production than Indian man.

EXHIBIT 61. Comparison of the heat production of individual Brown Swiss and Brahman heifers (top) and lactating Brown Swiss and dry Brahman cows (bottom) in relation to gradually increasing environmental temperature.

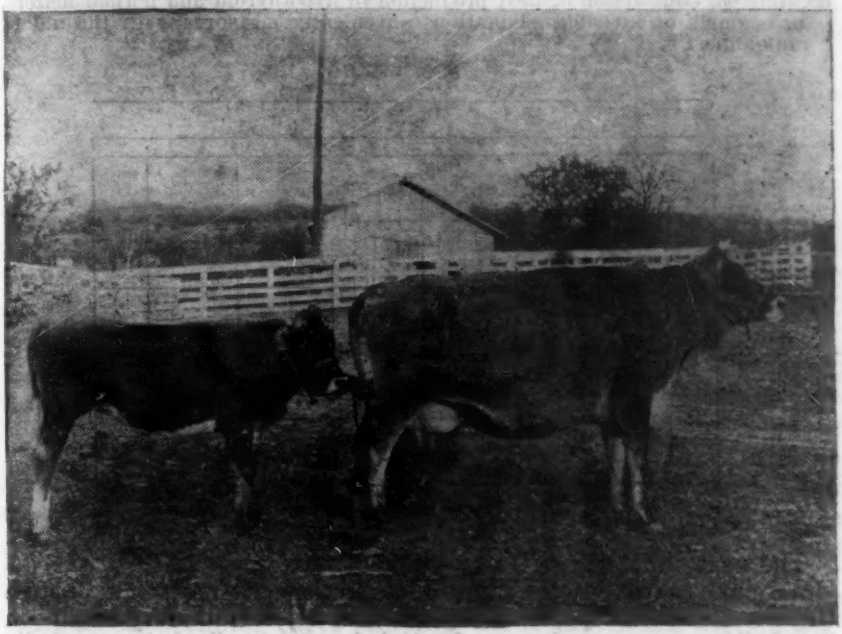


In the next slide I am coming to the radioisotope business with special reference to the thyroid gland. The thyroid gland is an extremely important endocrine gland, but it is not the only important one affected by temperature. There are many others, and they are all important and interrelated in a complex system. We chose the thyroid for study for reasons I will explain in a moment.

First, let us see how the thyroid is involved in growth, in milk production, in heat production, and therefore in heat tolerance.

The two animals shown on this slide (exhibit 62) are exactly the same age. Now look at the difference in size and development between the 2 animals at 2 years of age.

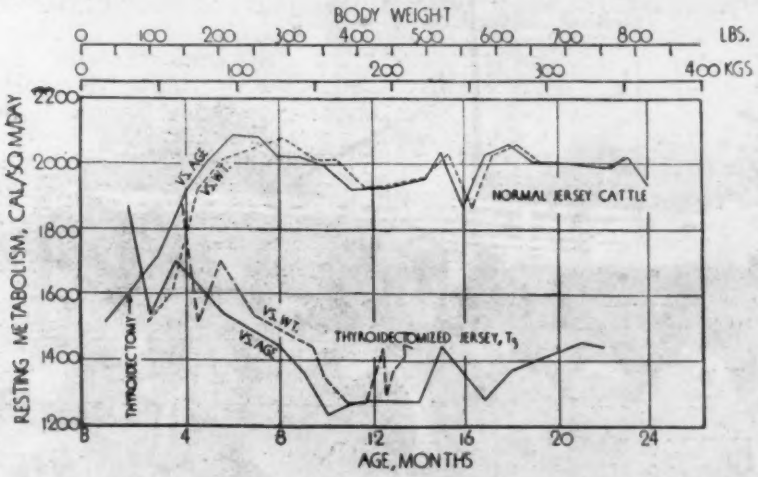
EXHIBIT 62. Comparison of the productivity (growth rate and milk yield) of thyroidectomized heifer and normal control. The neuroendocrine system, reflected in this case by thyroid activity, controls all life processes including agricultural productivity.



This small one, from which the thyroid was removed at 2 weeks of age, is stunted in body size and sexually infantile. The other, 2-year old, with its thyroid intact, is a large, well-developed normal cow. The thyroid is thus a very important endocrine (hormone-producing) gland. It is a link in the major neuroendocrine chain that controls the body machinery including growth and development, feed consumption and milk production, and we are working on that thyroid link in the complex neuroendocrine chain with the aid of a radioisotope.

The next slide (exhibit 63) shows the heat production, a very important aspect of life in warm-blooded animals. The heat production in the normal heifer at rest is seen in the slide to be 2,000 calories per square meter per day; in the thyroidectomized animal, only 1,200 calories per square meter per day. As I said, the thyroid is a link in an extensive neuroendocrine chain.

EXHIBIT 63. Comparison of heat production in hypothyroid and normal heifers, an example of invisible adaptation conveniently measured with the aid of radioidine, I^{131}.



The next slide, please.

We chose to measure the thyroid link in the endocrine chain because there is a radioisotope, I^{131}, which can be injected in very small—in "tracer"—amounts, and so used as label or "tracer" of the metabolic changes of the normal iodine, I^{127}, in the body, especially in the thyroid.

The procedure is to inject a very small amount of I^{131} into the jugular vein of the cow. Then we count with the Geiger counter, as shown in the next slide, and that way follow the time changes of the radioiodine, I^{131}, that has been injected.

The next slide, please (exhibit 64).

We determine the amount of radioiodine that goes through the thyroid by comparing the counts of a Geiger counter having the probe against the heifer's thyroid with an "artificial thyroid gland," simply a beaker containing a known amount of I^{131}.

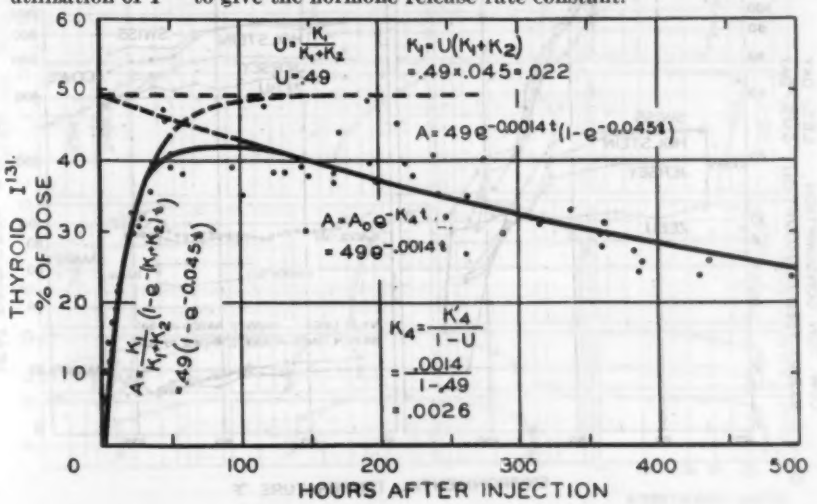
The next slide, please.

EXHIBIT 64. In vivo determination of thyroid I^{131}.

The injected radioiodine is taken up by the thyroid. The slide (exhibit 65) shows first a rise in the Geiger count (I^{131} is taken up by the thyroid) after injection, then a decline.

The slope of this rising curve is called k_1; we then measure the slope of the declining curve reflecting the release of the thyroid hor-

EXHIBIT 65. Thyroid I^{131} content. Rising segment shows uptake of I^{131} from blood; declining segment, release of the thyroid hormone containing I^{131}. Equations indiacte calculation of rate constants for those processes and calculation of the apparent hormone release rate constant, k_4. K_4 is corrected for reutilization of I^{131} to give the hormone release rate constant.

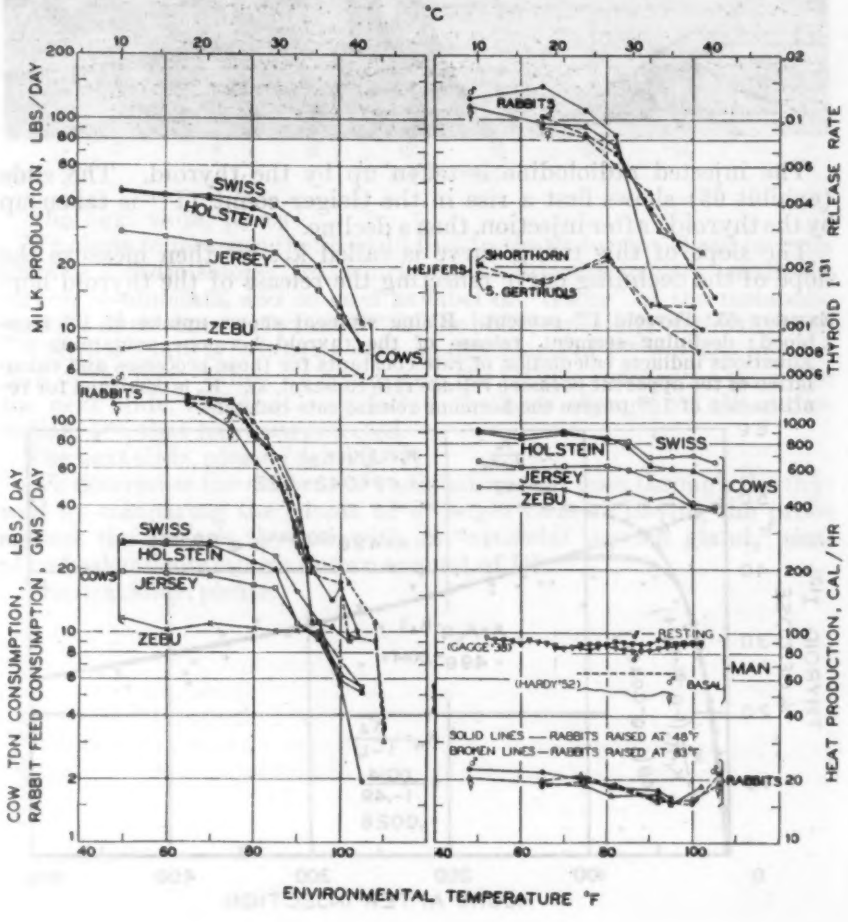


mone containing the I^{131}. We call the declining curve k_4. We also measure the top of the rising-declining curve, which we call U. The rate at which the thyroid functions (secretes thyroid hormone) is determined by the slopes k_1, k_4, and By U. The results by the three methods—by the slopes k_1, k_4, and U—agree.

The next slide (exhibit 66) shows the effect of temperature on the thyroid. When the temperature is 60° F., the thyroid activity is relatively high, so that the decline, k_4, in radioiodine is rapid; but when the temperature is 95° F., the curve is quite flat, the thyroid function is slow. Temperature is thus seen to have a profound effect on thyroid activity.

This slide also shows the relation between thyroid activity, milk production, feed consumption, and heat production.

EXHIBIT 66. This arithlog grid shows the similarity in shape between the curves for thyroid activity, feed consumption, milk production, and to less extent heat production in cattle and rabbits. Being thus interrelated, thyroid activity in young females and in males, too, may be used for predicting milk production potentialities. The heat production curve for man was inserted to indicate some basic differences between cattle and man in reaction to temperature. Man does not show breaks in the curves at 80° F.

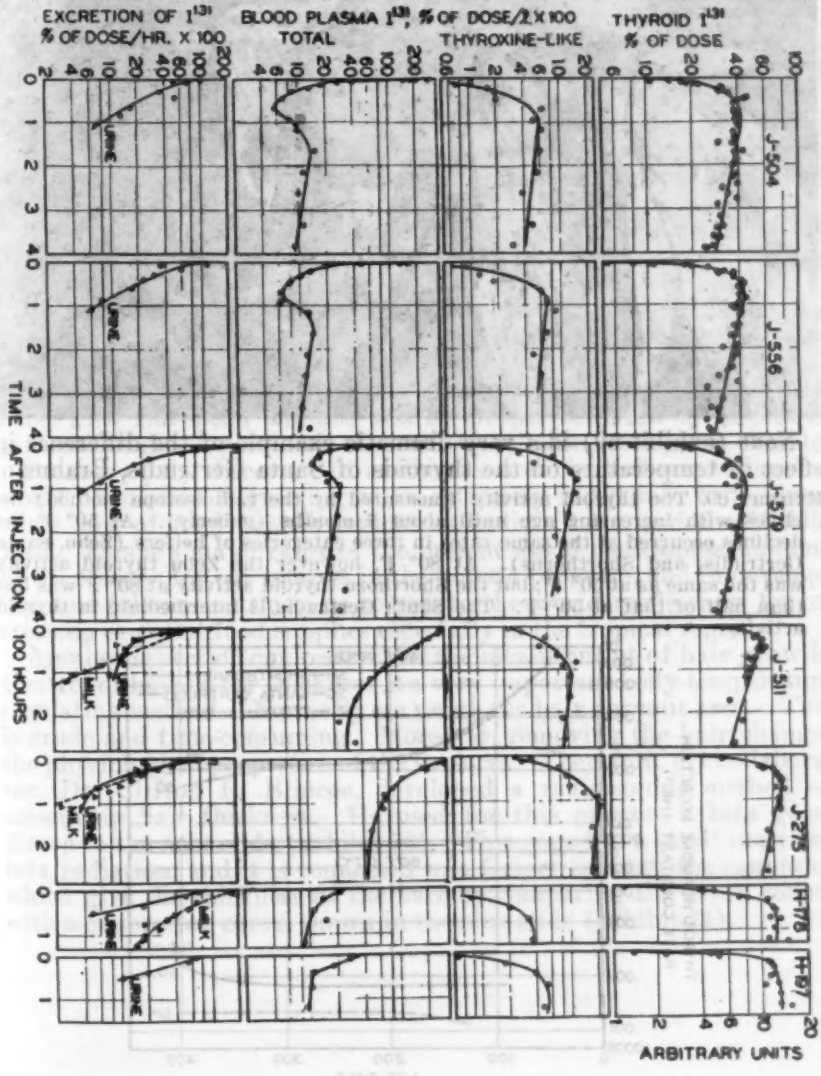


The feed consumption begins to decline in European cattle beginning at 80° F., as does milk production, thyroid activity, and heat production; 80° F. is thus a critical temperature for European-evolved cattle as Holsteins and Shorthorns. We may thus measure the productivity of cattle (production of milk or beef) by thyroid activity.

By way of comparison, man's heat production is also shown in this slide. While the heat production in cattle declines at temperatures 80° to 105° F., man's heat production is not affected by such rise in room temperature because man has a relatively much better cooling (sweating) mechanism than cattle.

Next is a rather complicated chart (exhibit 67) showing the various excretion paths of the injected radioiodine. One curve shows the path of movement of the I^{131} in the thyroid gland; another curve

EXHIBIT 67. Time relations of metabolism and excretion of injected I^{131}.



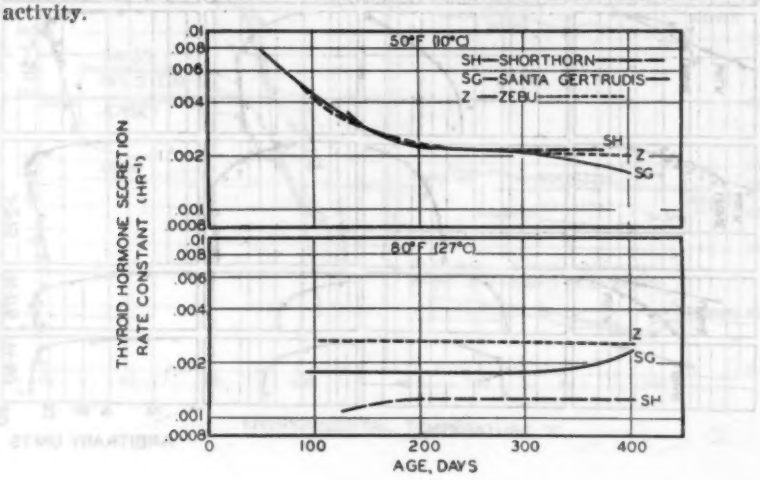
shows the loss of the I^{131} from the thyroid to the blood; a third curve represents the excretion of the I^{131} in the urine.

The next slide (exhibit 68) shows how the cow's urine is collected. The urinary I^{131} excretion is estimated by quantitative collection of the urine and counting for its I^{131}.

EXHIBIT 68. Urine collection by modification of the Hansard methods. Gasoline cans were used as receptacles.

Next (exhibit 69) is a very dramatic example of the difference in effect of temperature on the thyroids of Santa Gertrudis, Brahman,

EXHIBIT 69. The thyroid activity (measured by the radioisotope method) declines with increasing age until about 7 months (puberty). At 50° F the declines occurred at the same rates in three categories of heifers (Zebu, Santa Gertrudis, and Shorthorns). At 80° F, however the Zebu thyroid activity was the same as at 50° F; but the Shorthorn thyroid activity at 80° F was less than half of that at 50° F. The Santa Gertrudis is intermediate in thyroid activity.



and Shorthorn heifers. Here is the Santa Gertrudis; here is the Zebu; and here is the Shorthorn.

As the animals grow older, the thyroid activity declines—until about 6 months of age (age of puberty). Then it becomes fairly flat. In a 50° F atmosphere the thyroid activity goes down to the same level in the Zebu, Santa Gertrudis, and Shorthorn heifers. But at 80° F, the Zebu thyroid activity is the same at 50° F; the Santa Gertrudis curve is somewhat below the Zebu; the Shorthorn curve is much below that of the Zebu.

In other words, the thyroid activity is an excellent index of the way the animal is affected by temperature, and what it will do in the line of milk production and feed consumption under given temperatures.

To summarize our work on thyroid activity, we are interested in thyroid activity because it is a link in the neuro-endocrine chain which controls the rates of all life processes, including milk production, beef production, reproduction, and so on, and knowing the thyroid activity we can predict the other processes, including the agricultural productivity of the animal.

For example, we can predict the productive potentialities of a young calf and we also can tell the effect of temperature by measuring with the aid of radioiodine, I^{131}, the reaction rate of the thyroid to a set of temperatures.

Now, what makes the Zebu more heat tolerant than the Shorthorn? Some of the things I already mentioned: The Zebus have better ways for dissipating heat (large ears, dewlap, navel flap, short hair, etc.); they have a lower heat production. There are other mechanisms. We do not know them all. Therefore we would like to study as many processes and probable heat-tolerance mechanisms as possible so as to find out what makes the Zebu more heat tolerant; then cross-breed the Zebu with European animals and by proper selection in successive generations develop animals that will be suitable for a given climate.

Because of the discovery of antibiotics and chemotherapeutics, the world population is growing at an extremely rapid rate with consequent lack of food in such regions as India, China, and the Middle East. This is a major cause of the present world restlessness, and one of the reasons for our interest in the point 4 program, and in developing heat-tolerant cattle so as to reduce the world restlessness by increasing essential food supplies especially in the tropical regions.

Another aspect of our research is the measurement of hair growth. Control of hair or fur thickness is a very important body-temperature regulating method. Normally we weigh the hair per unit area. This is crude and time-consuming. Moreover, removing the hair changes the physiological properties of the surfaces. Therefore, my collaborator, Dr. Clifton R. Blincoe, developed a radioisotope method of measuring hair thickness. He used for this purpose a beta gage, shown in the next slide (exhibit 70). This gage has a small source of beta radiation, and it is connected to a Geiger counter, the counts of which give the thickness of the hair by comparing the given counts with a calibration curve, shown in the next slide (exhibit 71).

EXHIBIT 70. Beta gage for measuring hair density.

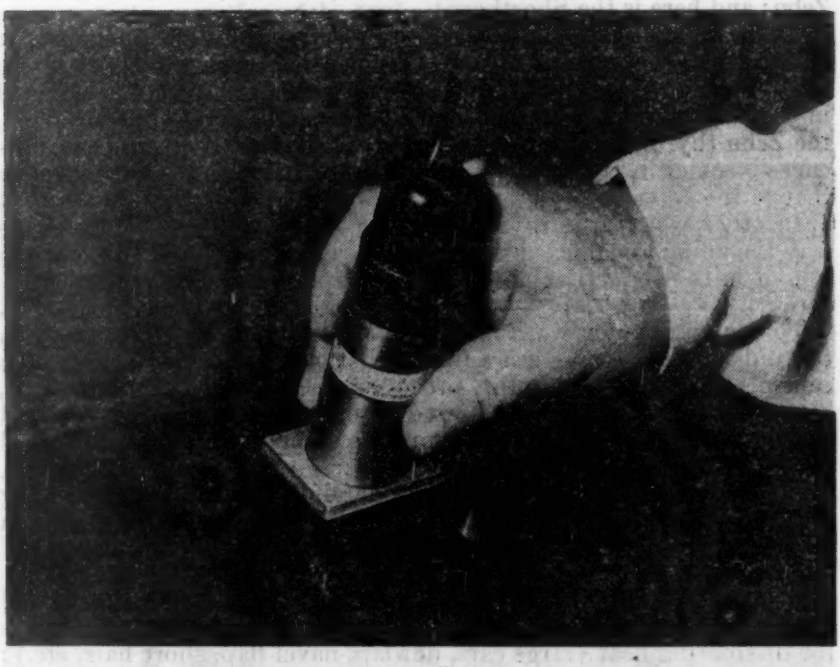
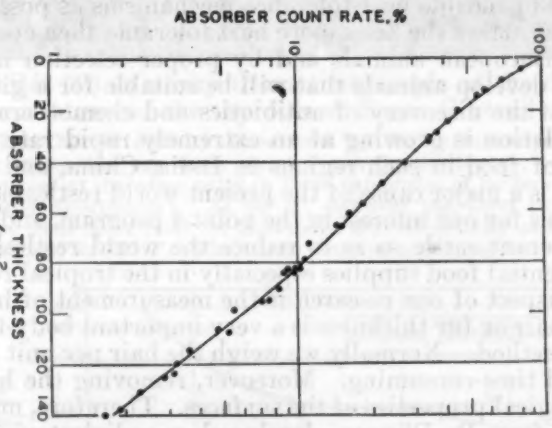


EXHIBIT 71. Calibration curve for a Tl^{204} hair measurement beta-gage. This curve is constructed using calibrated aluminum absorber and verified with hair.



This is the story, as far as we have gone in the use of radioisotopes in the Climatic Laboratory in Missouri. It is just a beginning, but gives an indication of what we hope to accomplish.

We also measure blood-cell volume; water in the various bodily compartments, cellular water, extracellular water, blood serum, and so forth with the aid of radioisotopes. They are all involved in body-temperature regulation. We can measure almost any element or any compound in the body by "labeling" it with any appropriate radio-

isotope. Our most substantial results were, however, as explained above, on measuring thyroid activity in relation to temperature and productivity. This, then, is my background statement on the work in the Climatic Laboratory in Missouri. A fuller and more orderly statement is given in the mimeographed copy submitted to Dr. Boss of the AEC.

Thank you very much.

Senator BRICKER. I have just one question, Doctor. You mentioned the productivity and the resistance to heat are particularly determined by the functioning of the thyroid and production of thyroxine. That in turn is controlled by another, being the pituitary gland; and back of that is the pineal?

Dr. BRODY. No. The pituitary is controlled by the hypothalamus—a vital link in the central nervous system. The thyroid is controlled by the pituitary and the pituitary by the hypothalamus. More generally speaking, all glands and tissues are interrelated links in a complex neuro-endocrine-somatic system, all dependent upon each other; but some, like the pituitary, hypothalamus, thyroid, and adrenals, received more study than the others and so more is known about them.

Senator BRICKER. You used as a gage entirely though your thyroxine as produced by the pituitary, carried out by the thyroid?

Dr. BRODY. We used the rate (steepness) of decline of the injected radioiodine in the thyroid as a gage of thyroid activity which is under the control of the pituitary, in turn is under the control of the temperature-regulating center in the hypothalamus.

Senator BRICKER. What is the relation of the pineal?

Dr. BRODY. We lack knowledge about the function of the pineal in spite of dramtic claims by a Dr. Rowntree to the contrary. I have a feeling that an assistant played a practical joke on the professor which led to the claims of the importance of the pineal.

Senator BRICKER. However, there is such an endocrine gland hidden way back?

Dr. BRODY. Yes, there is such a gland, but we do not know its function.

Representative VAN ZANDT. Doctor, this all results from the use of radioiodine; is that correct?

Dr. BRODY. We used radioiodine for obtaining data on the rate of thyroid activity. The rest of what I said is interpretation of the data to problems on body temperature regulation and on productive processes.

Senator BRICKER. That is just a measuring scale?

Dr. BRODY. That is correct. The rate of movement of the radioiodine through the thyroid gland is used as a measure of the rate of thyroid activity.

Representative VAN ZANDT. It is a tracer?

Dr. BRODY. Yes; the radioiodine is used as a tracer for following or measuring the rate of production and release to the blood of the thyroid hormone (thyroxine).

Representative VAN ZANDT. And you apply it to the thyroid of the animal?

Dr. BRODY. Yes, sir. The rate of thyroid activity is measured by the movement of the radioiodine as a tracer by applying a probe (con-

nected to the Geiger counter) to the neck of the animal nearest to the thyroid.

Representative VAN ZANDT. Does this in any way retard the growth of the animal?

Dr. BRODY. No, the amount injected is in tracer doses, that is, in insignificant amounts. It does not affect the animal. If you would inject a sufficiently large dose, it would destroy the thyroid. Indeed, injection of massive doses of radioiodine is used for destroying cancerous thyroid tissue.

Representative VAN ZANDT. We have talked about 80° F. and 50° F. What about the effect of 100° F. in countries like the Middle East?

Dr. BRODY. The existence of 100° F. temperatures is a very serious problem in tropical regions as in the Middle East, or India, some South American regions or even in our humid Southern States. This is, of course, the practical—humanitarian and diplomatic—reason for our interest in this problem. Our European-evolved cattle collapsed at environmental temperature of 105° to 110° F. and 70 percent humidity. The precise effect, however, depends on the humidity of the air, on the diurnal temperature rhythms and as explained, on the breed of cattle. If the nights are very cool, even European-evolved cattle tolerate very high midday temperatures, because of their high heat capacity, for a few hours.

Representative VAN ZANDT. Can you see in the future when it may be possible to develop an animal that will be able to exist on the Equator and grow in the same proportions as these animals you have referred to?

Dr. BRODY. Yes, sir, provided that "philosopher kings," like the Klebergs, who combine power (money), knowledge, wisdom, and continuity of policy in successive generations undertake this task. To succeed in such an enterprise, one must have not only knowledge and wisdom, but also something like the mentioned 300 bulls to select from in the breeding operations. However, the results from the isotope experiments may give a basis for assaying the hereditary potentialities of individual animals so there will be less need for having such large populations for selection.

We cannot, at the State experiment station, do very much of such breeding because we do not have the money nor the long-range continuity of policy but we can study the climatic physiology of cattle so that those people who do have the combination of power, resources, knowledge, wisdom, and continuity of policy may utilize this knowledge for developing the proper kind of cattle. We need more institutions like the King ranches for developing dairy cattle, as milk is a more economical essential food for the poor and hungry than is meat.

I might say that the Klebergs are not supporting our work. They only contributed animals for the experiments, for which we are very grateful.

Representative VAN ZANDT. Doctor, as to the radiation that is contained in the iodine, at what portion of the body of the animal does it center?

Dr. BRODY. It centers in the thyroid.

Representative VAN ZANDT. Does it stay right there?

Dr. BRODY. No, it moves rapidly as shown in the slide, reaching a maximum within 24–72 hours, then going down and out in the urine.

Maybe we can use radiosodium for tracing the movement of the blood from the body interior to the periphery or exterior where it is used for evaporative-cooling purposes. I do not know. We are in the beginning stages of this research. There are all sorts of possibilities. Almost every element and almost every compound in the body may be similarly labeled with appropriate isotopes for following them in their metabolic transformations.

Representative PRICE. Thank you very much, Dr. Brody.

Dr. DUNHAM. Mr. Price, the next scientist who will present a report is Dr. Arthur D. Hasler, professor and chairman, department of zoology, the University of Wisconsin.

Dr. Hasler is going to speak about the use of radioisotopes and atomic energy in the service of marine and fresh-water agriculture.

STATEMENT OF DR. ARTHUR D. HASLER, PROFESSOR, DEPARTMENT OF ZOOLOGY, UNIVERSITY OF WISCONSIN

Dr. HASLER. Mr. Chairman, gentlemen of the Congress, Dr. Dunham and fellow citizens, we are concerned on a worldwide basis with the food of the world and it is a rather striking paradox that while 70 percent of the earth's surface is water, only about 2 percent of the protein of the world comes from the water.

Senator BRICKER. Consumed protein?

Dr. HASLER. Consumed protein. On a worldwide basis, only 2 percent of it comes from the oceans, and the other paradox is that when one studies the production of the oceans with radioisotopes, such as C^{14}, one arrives at a production figure of total organic matter of approximately 3 tons, which is probably of the order of magnitude of production of our most productive forests. The organic matter is there to be used.

The problem is how to use it most efficiently. Let me just give you a few introductory figures on the amounts of food that come from our various fisheries, as compared to farming. In this table (exhibit 72) are pounds per acre harvested per year. The rich Wisconsin pasture will probably produce 190 pounds; poor range, 20; western range about 3. The dairy farmer is the best in protein production, reaching 1,200 pounds if you correct for the water content.

EXHIBIT 72

Annual yield of meat from various types of waters compared with harvests from land

Farming (Temperate Zone)	Meat produced pounds per acre per year
Grazing (beef the only product):	
(a) From rich pasture	190
(b) From poor pasture	20
(c) From western range	3
Dairy farming:	
(a) Milk	[1] 1,200
(b) Meat	45
Total	1,245
	Carbohydrate, pounds per acre per year
Mixed arable farming (various arable crops grown):	
(a) Wheat	1,950
(b) Potatoes	17,920
(c) Sugar beet (as sugar)	3,043

Type of fishery	Meat produced pounds per acre per year
Large waters:	
Great Lakes	1–8
Georges Bank, Mass	20
North Sea	50
Tropical oceans	?
Small lakes:	
Alpine lakes, Europe	7
Lake Mendota (deep, fertile)	100
Waubesa (fertilized, shallow)	300
Ponds:	
European carp ponds:	
Natural	100
Fertilized	300
Southern United States bass ponds:	
Natural	120
Fertilized	500
Tropical carp ponds:	
Natural	400
Fertilized	1,500
Artificially fed	3,000

[1] Corrected for differential water content of meat versus milk, that is, where 2,000 pounds is whole milk.

The dairy farm produces around 1,200 pounds of protein per year. Compare that with carbohydrates, which go considerably higher, potatoes up to 17,000, sugar up to 3,000 pounds. It is in this order of magnitude that the ocean produces if you compare the "grass" of the ocean with the grass of the land.

Here are the Great Lakes: 1 to 8 pounds per acre, so therefore the Great Lakes are relatively poor producers of protein and compare better with western range. North Sea, 50 pounds, is the most productive of the seas. We have very little knowledge of how much the tropical ocean produces, so that is questionable.

Some of the small lakes, 7 pounds; Lake Mendota (site of the University of Wisconsin), 100 pounds, and the lake that receives the sewage in the city of Madison, well fertilized Lake Waubesa, reach about 300 pounds.

The European carp ponds and ponds in the Middle East and China are very important producers of protein.

The people in these areas are short of protein. Some of them don't like to eat Dr. Brody's hybrid cows or have some aversion to eating cattle meat, that is, nonfish animal meat.

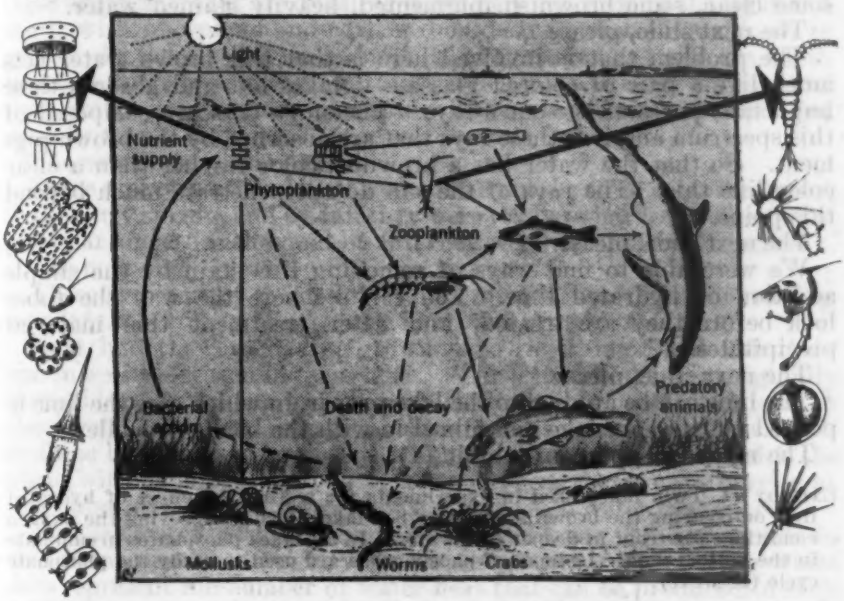
Fish is a very important item from a social and psychological point of view in these areas. The natural pond in Europe will produce about 300, the fertilized pond 300, southern bass ponds, around 120, and fertilized about 500.

In the tropical areas where the growth is continuous throughout the year you have very much higher figures. As much as 1,500 pounds of carp may be produced in southern China, or in India, or in Israel, that is, tropical area of that type.

We have here the potential, it appears, at least in the pond area, for matching the production on an acre-to-acre basis with the best types of land farming. In the seas it is a big question mark owing to selection and intensity of harvesting. I will discuss this point a little later.

I would like first, then, to go briefly into how food is produced in water. The complex story of getting the energy from the sun to the fishes is as follows: The energy is taken up by these microorganisms which can only be seen by a microscope. They have, through the enlargement of the microscope, this anatomy (exhibit 73). These are all microorganisms belonging to the group called algae or diatoms.

EXHIBIT 73. Food chains in the sea. Energy from the sun and nutrients are used by microscopic plants (algae). These in turn are eaten by water fleas, and these by fish (see text).



These are in turn fed upon by animals a quarter to a half inch in size, and these are fed upon by the small fishes and then the small fishes by the big fishes. Some of these algae and bigger forms are not eaten but fall to the bottom and are consumed by worms, snails, clams, and other organisms. This is a complex food chain in the sea and the loss of energy in each one of these links is very important. I believe this is also an area where we can expect some contributions from the use of isotopes in discussing what the efficiency in these food chains might be.

For instance, it might be possible to determine, by having the isotope taken up by these diatoms, what percentage is passed on to the organism that eats the diatom and what percentage of that is passed on to the one that eats this one. We might be able to work out efficiency rates, and if we are every hard pushed for food from the sea, it may be more sensible, for instance, to take food out at this end of the link rather than waiting until it goes through to the fish.

In the lakes of our area, of which there are some 5,000 named lakes in Wisconsin, and in Minnesota, Ontario, and Michigan still more, we can observe similar processes. The sun's energy penetrates the water and is used by the diatoms and other algae. Those in turn are eaten by the water fleas, water fleas by some of the insects, insects and water fleas by the little fish, little fish by the bigger fish, and so

forth, some of them eating the worms on the bottom which again live on this food which rains down from the upper layers. At this junction, I would like to pass to some experiments that we are doing at the University of Wisconsin on our lakes in the northern part of the State. Here we have an experimental site in the out-of-doors.

These are all colored slides. Apparently they are not going to be visible if we can't darken the room. Try the next one, please.

One of the problems in many of the small lakes in northern Wisconsin is the color of the water. Some might be a bright yellow; some clear, some brownish, pigmented, heavily stained water.

The next slide, please.

The problem that is involved here is that this brown water acts much like a pair of colored glasses—it takes out and absorbs these important parts of the sun's rays. The sun's rays are composed of this spectrum and it is these rays that are absorbed by the brown pigment. So that the water has a brownish color rarther than a clear color like this. The rays of the sun do not penetrate much beyond this point.

The next slide, please.

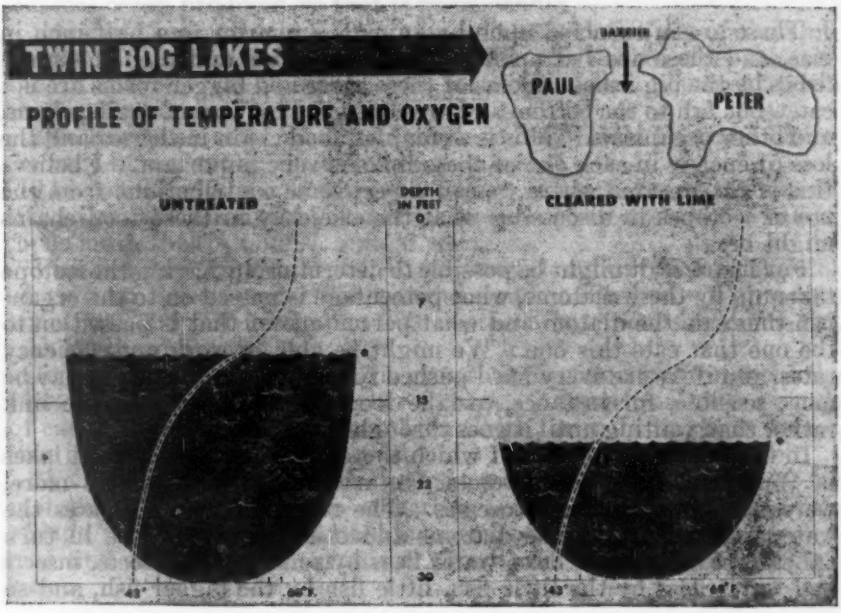
We were able to find ways of removing this stain by the simple addition of hydrated lime. You can see here the way the tubes look before they are treated, and after treatment this material precipitates.

The next slide, please.

The lime can be applied to the lake proper, in which case the lime is poured out into the lake and mixed in with the boat's propellers.

The next slide, please (exhibit 74).

EXHIBIT 74. Twin lakes used in experiments for testing the effect of hydrated lime on clearing the brown stain from bog lakes, hence improving the oxygen conditions for trout in deeper cool water. In all lakes phosphates accumulate in the bottom mud. Isotopes of phosphorous are used to study the phosphate cycle (see text).



In the crucial experiment, I was able to locate a lake in northern Wisconsin which had a natural constriction in it. At this particular point by getting a bulldozer in there and filling in a barrier we were able to create an experimental and a control lake—one which we would treat with hydrated lime to reduce the color and one which would remain as a control, untreated.

You can see here the results of that treatment. In the untreated lake the light only penetrates to this level, and the treated lake is penetrated to this level. So there is a doubling in the light and therefore these organisms that are dwelling down here can pick up the light and use it with phosphate and carbon dioxide to produce algae down to greater depths, so that the basic grass of the lake has twice the depth in which to grow and that, in turn, gives an opportunity for more of these water fleas to grow and feed. The water fleas in turn are fed upon by trout.

The next slide, please.

These are some of the lakes in which we put the trout after treatment in the early spring, and by fall they were ready to harvest. They were put in at about 5 inches and by fall they were about 12 to 14 inches.

The next slide, please.

These are some of the delightful operations involved in harvesting some of those trout. We can also harvest them with nets.

Next, here they are, having grown up to something like double their size in a single season in these lakes. This type of lake was originally incapable of producing trout because the light only penetrated down to this level. This water in here is cold. There is no oxygen at this depth in these brown lakes because the light can't penetrate to furnish the algae with enough energy to produce oxygen, therefore a barrier at this point prevents trout from getting to the cold water in summer.

If it is treated with lime and cleared, the trout will have access to this point and produce very handsome growth. These little white dots represent the number of water fleas that can be produced in such a lake.

Throw that one slide back in again.

Representative VAN ZANDT. Can you compare the growth of those trout with the conventional type trout?

Dr. HASLER. That is right. They grow about like they would grow in a hatchery in one of these lakes.

These water fleas are so small that one has to use this straining device to capture them. You can lower this straining device to different levels in the water and move horizontally around in the lake, capture the water fleas and measure the amount produced.

The same type of gadget is used in marine fisheries to determine the amount of food which is available for the fish which eat these little animals.

We find in these lakes one of the uses of atomic energy, the use of isotopes, and we are now, having gotten to the point where we can improve the light penetration, we are now working on the possibility of improving the phosphate or fertilizer situation.

We find that in these lakes, in all lakes in fact, even Lake Mendota, and in the ocean, phosphates are taken out and precipitated to the bottom by these rain organisms which have captured the phosphorus in the upper waters and carried it to the bottom.

We find a very small percentage of this phosphate actually ever gets to the surface again. The large majority of the phosphorus stays in the bottom mud, unavailable to the top. We have been able to put radioactive phosphates in the surface water and follow their movement down to the bottom.

Then we have been able to pump this water at the bottom which is rich in phosphate, by ordinary irrigation pumps, to the surface, and fertilize the surface again. We have also introduced a phosphate into the bottom water and allowed it to become incorporated in the bottom mud. We have devised a harrow, like you use a harrow on the farm, which we drag along the bottom so that great "clouds" of this rich phosphate organic material swirl up. When the "clouds" are produced water is again pumped to the surface to fertilize the surface water and to increase the amount of fish food organisms.

Representative VAN ZANDT. With respect to the phosphorus that you placed on the bottom and then brought to the surface, was it the same type of phosphorus that you deposited on the surface and it filtered its way down?

Dr. HASLER. That is right.

Representative VAN ZANDT. Did it have the same strength?

Dr. HASLER. The phosphorus decomposes at a rather rapid rate so that that has to be charted. You know, every day after you put this in, how much is lost by natural decay and how much is left so that you can correct for that factor by the conventional tables.

We are going to try to harrow this summer and then produce very heavy bubbles near the bottom to see if we can bring that phosphate which is very tightly bound to the organic particles to the surface and thus fertilize the surface water.

The point here is that these lakes are, as are the oceans, really wasteful as far as phosphorus is concerned. If one were to import fertilizers for these lakes, import the phosphorus, say, from other parts of the country, it would be at considerable expense. However, if one could reuse the phosphorus already in the lakes to fertilize them it is my opinion that this would be an advance in this type of lake management.

This would be a conservation measure and since we eventually expect to have less and less phosphorus from our existing geological deposits as it is used up for fertilizing purposes, it will become more and more important to reuse the phosphorus in the lake bottoms.

The lake will collect the phosphorus from its basin and, depending on the size of the watershed around a lake of this type, it runs in with the rains and is continually precipitated to the bottom.

The use of these isotopes is helping us to understand better the reuse of this material.

It might be added that the phosphates that do go to the bottom are very insoluble. We have tried to treat the mud with lime, which is a common practice in treating acid soils. It so happens in these lakes the phosphorus becomes more tightly bound after treatment with calcium carbonate.

If you acidify the water you can get phosphorus released to some extent, but then you kill the organisms upon which the fish feed. There is work to be done to find some way of chemically treating this bottom mud so it will release the phosphorus more readily.

We found by a radioactive technique that if you have a column of water—this column, for example—over a column of mud, and you

introduce phosphate that is radioactive at various levels in the mud, you will find that the phosphate that comes out of the mud must be practically in contact with the surface. This fine film here about a centimeter below the surface of the mud is the lowest point from which it will leach into the water.

If you put the phosphorus phosphate in at least 2 centimeters below—in other words, have it an inch below the surface of the mud—practically no phosphate leaches back in. This is one of the reasons why we did the harrowing experiment, to produce these clouds of ooze, and then pump the water to the surface where it would be taken up by the algae, which in turn would complete the food chain we were talking about earlier.

I would like now to make some rather provocative suggestions as to other possible uses of atomic energy in hydrobiology which might result in increasing the harvest of proteins from the sea. I have mentioned already the uses of carbon-14 in measuring total production in the sea. There is also the possibility of using some of the radioactive isotopes in following these food chains to find out which is the most efficient part in which to tap the energy, also we need more knowledge about how a fish ticks. When you realize the complex physiology of the cow, as has been told to us by Dr. Brody, one must realize that we know much less about the fish. The marine laboratories studying physiology of fishes could give us a great deal of information on the metabolism of fish and give us a better understanding of fishes and fish products if the use of radioisotopes were used more intensively.

One suggestion that I have thought of in connection with the use of atomic energy would apply to the "have-not" nations such as India or Japan, where their ships have to go rather long distances into the tropical seas to harvest the crop of fishes, such as the tuna. If these ships are at sea for very long in warm climates the fish spoil.

They have two factors to deal with, the distance to shore and the refrigeration of the fish once they have them on deck. I visualize the possibility of being able to build an atomic ship, something on the order of the *Nautilis*, with an abundant supply of energy available for the canning and refrigeration processes that could be taking place on the ship as soon as the smaller fleet ships which supply such a mother ship landed their catch of fish.

Furthermore, there would be on such a ship sufficient energy to have large refrigerating rooms and these refrigerating rooms, as I visualize it, would be of sufficient size and have sufficient electrical power to keep them refrigerated for many weeks until they had a full load.

One of the big hazards of the tropical fishery is the spoilage process of the fishes after they have been captured. The fish could be sterilized by the process described earlier by Dr. Schweigert. Another rather far-reaching suggestion would be the possibility of having such ships equipped with sufficient power so that they could generate enough electricity for attracting fish to a concentrated area.

I visualize that such a ship, after locating a school of fish with echo sounding, could put out the electrodes with these rather tremendous amounts of energy that would be required in the ocean to assemble these fish, pull them together into a "ball" with direct current, and then pump them onto the ship, filter out the fish, and in

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that way cut down some of the time factors in capturing fish through the conventional techniques.

This is, I am sure, far reaching. It has been suggested by some of the German workers and they have worked on the electrofishing techniques. There seem to be a lot of unsolved problems there, but one of the big problems is energy; like in the previous suggestion, such an atomic ship would have tremendous quantities available.

Another suggestion that I thought might be provocative and of some conservation use is one connected with the fact that we know that the salmon is declining on our west coast. On our east coast the salmon has declined to almost a negligible fishery.

One of the contributing factors is the competition that the salmon has with the irrigation and power dams. One important point about that is that while fish can be circuited around the dams by fishways en route to spawn except those that are very high, such as the Grand Coulee Dam—the young cannot get back as safely. The adult salmon in migrating home will pass around the dams via the fishways, but in moving back after spawning is where the big losses occur; that is, in going through the turbines from the reservoir part of the dam to the other side. Here there are rather heavy mortalities in the young salmon returning to sea.

It seems the biologists and engineers working on this problem have been unable to solve the question of how to direct those young fishes, once they have reached the reservoir above the dam, so that they are not killed in passing from one side of the dam to the other. The more dams you put in a stream the more mortality there is.

I visualize this necessity: That biologists and engineers need a moratorium at some proposed dam site to give them time to work out this very difficult problem of the behavior of the salmon and how to get him around these dams.

If one could build an atomic-energy plant at such a proposed dam where there would be enough power to equal the power that would be put out by the proposed dam, then this energy from atomic energy in making electricity would replace the original need for this study period in which we would attempt to solve the problem of getting the fish around the dam.

Certainly some day we will need both—the power of the streams and the power of atomic energy—but at least this would give us a moratorium in which to study this problem and see if we can solve it.

I think it is soluble if we have enough bright students working on it.

The last suggestion I have is the possibility of the use of atomic energy for a city, say, the size of Chicago, for warming the sewage.

In the temperate zones of the world the cold weather is responsible for a rather slow sewage-treatment process. The cool weather and cold waters that are used at that time of the year reduce the efficiency with which the sewage is decomposed or broken down. In the summer it is hardly a problem and my suggestion here would be the possible use of the heat from atomic-energy plants to warm the sewage in such a way that you would get better decomposition and, therefore, improve the sewage-treatment process.

Thank you.

Representative PRICE. Thank you very much. Do you have any questions?

Thank you very much, Dr. Hasler, for your presentation. It was very interesting.

Dr. Dunham?

Dr. DUNHAM. We have now Dr. Edward F. Knipling, Chief of the Entomology Branch, Plant Industry Station, Department of Agriculture, Beltsville. He is going to present a report on the use of radioisotopes in the field of entomology.

Representative PRICE. Dr. Knipling?

STATEMENT OF DR. EDWARD F. KNIPLING, CHIEF, ENTOMOLOGY BRANCH, PLANT INDUSTRY STATION, DEPARTMENT OF AGRICULTURE, BELTSVILLE, MD.

Dr. KNIPLING. Mr. Chairman, I appreciate the opportunity of appearing before this committee to discuss this subject, the use of atomic energy in furthering entomology research and insect control.

I know that time is limited and I have a prepared statement in which I go into some detail on the various types of investigations that are furthering insect control, but I believe I will just briefly summarize some of these investigations so I will have more time to discuss in detail the possible eradication of the screwworm and possibly other insects by the release of male insects that have been made sterile by exposure to gamma rays.

Representative PRICE. You could summarize and go into the details of the more interesting experiments you are working on and we will include the complete text of your statement in the record.

(The statement referred to follows:)

STATEMENT OF E. F. KNIPLING, CHIEF, ENTOMOLOGY RESEARCH BRANCH, AGRICULTURE RESEARCH SERVICE, UNITED STATES DEPARTMENT OF AGRICULTURE

ATOMIC ENERGY IN INSECT RESEARCH AND CONTROL

I am pleased to have the privilege of appearing before this committee to discuss atomic energy as it relates to insect research and control.

The use of radioactive tracers represents one important application of this energy source. These tracers are furnishing new techniques that are of material value in advancing our knowledge of the biology, ecology, and habits of destructive pests. They provide a new tool for a better understanding of the way that insecticides control insects and how insecticides can be used more safely. Irradiation is another and more direct use of atomic energy. Bombardment of pests to damage their genetic makeup is being investigated as a way to actually control or eradicate certain insect pests.

Importance of insects

There are in this country more than 10,000 species of destructive insects. Worldwide, this number is multiplied several times. Some of the more serious diseases of mankind are transmitted by insects and related pests—ticks and mites—and as a group, the insects are man's chief competitor for the food, feed, and fiber that we produce. The agricultural economy of this Nation and the world would soon collapse if the many pests attacking agricultural crops were not adequately controlled. But in spite of the progress that has been made in controlling insects, it is estimated that in the United States their loss damage and the cost of control amounts to $4 billion annually.

Not all insects are harmful. Without the honeybee and other insects that pollinate plants many of our leading crops could not be grown profitably. In the absence of the parasites and predators, which help to keep insect populations in reasonable balance, the world would soon be overrun by insects.

This brief review of the economic effect of insects on the world's agriculture and their role in the health of man and animals, points up the importance of

atomic energy as a tool of entomological research and as an insect control weapon.

Isotopes as an aid to entomological research

One of the basic requirements in developing ways of controlling destructive pests is to obtain information about their life and habits. How does an insect spread? Why does it migrate and how far will it fly? How long will it live? What is the population density of various pests? Answers to these seemingly simple questions are vital if we are to control certain pests, particularly those that carry diseases to plants, animals, and man. Insects made radioactive by feeding or painting them with radioactive chemicals, then released and subsequently recovered in traps or by other means can be easily identified by exposing them to radio scalers such as the Geiger counter. Through this technique we have found that the housefly, one of our prevalent insect disease carriers, may migrate as much as 20 miles and that blow flies, important pests of livestock, will migrate at least 28 miles.

In connection with efforts to eliminate the screwworm from localized areas by releasing sexually sterile males, which I will discuss in more detail later, it is essential to first determine how many of the insects normally occupy such an area. By releasing a known number of radioactive screwworm flies in the area and by comparing the ratio of nonradioactive to radioactive insects caught in traps or on animals, it is possible to estimate the density of the natural population.

These are examples of the type of ecological investigations that have been advanced through the use of atomic energy. Such research as this which in the years ahead will add much to our basic knowledge of destructve as well as beneficial insects will become of increasing value in meeting insect problems.

Currently, the use of insecticides provides the most practical way to control most of our insect pests. The many new organic chemicals which in the past 15 years have proved to have great insecticidal merit have saved many millions of dollars and have prevented untold illnesses among man. Yet many problems arise in connection with the use of insecticides. One is the residue problem. We must determine how to use insecticides to control pests on agricultural commodities without leaving hazardous amounts of insecticide residues on harvested foods. Pharmacologists who study the toxicity of the pesticides determine the maximum amount of each pesticide that can be safely tolerated in the diet. They have found that some of the most effective insecticides are so hazardous that residues must be limited to 1 part in 10 million parts of food to be safe. The problem of detecting the minute amounts of such residues is one of the major obstacles in the development of new pesticides. Pesticides containing a radioactive label, however, provide a valuable tool for determining if residues appear in plant products, and in meat, milk or eggs.

Another serious problem connected with the use of insecticides is the development of insecticidal resistance by insect pests. Many investigators believe that this problem can be solved only by first obtaining basic information on the mode of action of insecticides and the mechanism of detoxification which permits resistant strains of insects to tolerate increasing amounts of insecticides. The use of insecticides containing a radioactive label are advancing such investigations.

Promising types of insecticidal chemicals are the systemic chemicals, which are absorbed through the roots, stems, and leaves into a plant's sap stream and then distributed throughout the plant. Systemic insecticides show similar promise in the control of insects that attack livestock; for example, cattle grubs, ticks, lice, and bloodsucking flies. By tagging these systemics with radioactive tracers, scientists have a tool with which they can determine the mode of action of these materials as they are absorbed and translocated by plants and animals.

Destruction of insects in infested commodities

The possibility of utilizing atomic energy for the control of insects by exposing insects directly to irradiation has been given considerable study. Investigations concerned with insects that attack stored products have shown that exposure of insect-infested grains to gammo rays from radioactive cobalt (cobalt 60) disrupts the life cycle of the insects. Success was achieved with dosages of less than 10,000 roentgens.

Another direct use of irradiation in insect control is to prevent the spread of insects to new areas. Perhaps the most common means of insect spread, particularly from one country to another, is through the shipment of insect-infested commodities. For example, the Mediterranean fruitfly which is now threatening the Florida fruit industry probably reached the United States in infested

fruit. To permit insect-infested commodities to enter commerce without danger of spreading pests to new areas, it is essential that there be available effective ways to first destroy the infestations. Fumigants and steam sterilization are now the principal ways to kill insects in commodities under quarantine regulations. These treatments are sometimes damaging to the commodities, and the use of fumigants may also be restricted because of residue problems. Research now indicates that it may be possible to use irradiation to destroy insects infesting fruits and vegetables. In Hawaii, where United States Department of Agriculture research is underway on several important tropical fruitflies, gamma rays from cobalt 60 have been shown to destroy the eggs or larvae of these insects infesting fruits. Exposure in the range of 10,000 to 20,000 roentgens will prevent insects from maturing. The treatment may not kill the insect immediately; however, death results before the insect reaches the pupal stage.

Enough information has been gathered to show that many insect pests can be killed directly by atomic irradiation. The practicality of this method will largely depend on the solution of engineering problems, taking into consideration the costs and hazards as compared with those of other control methods.

Screwworm eradication through release of sexually sterile males

The greatest advance in the utilization of atomic energy for the practical control of an insect has been made against the screwworm by saturating a screwworm-infested area with male screwworm flies made sexually sterile by exposure to gamma rays. With your permission I would like to take the time to go into some detail in discussing this development. Not only is it a unique approach to the control of an insect, but it may be the means whereby the can eliminate one of our worst livestock pests from Southeastern United States. Further research may show that the method will be useful against a few other important insect pests.

The screwworm is the larval stage of a fly about three times as large as the ordinary house fly. The fly (exhibit 75) lays its eggs (exhibit 76) on wounds of livestock and wild game. It will attack any warmblooded animal, sometimes even man. When the eggs hatch in the wound, the tiny larvae or maggots feed on the tissues of the animal. The maggots grow to full size in about 5 days. They are more than a half-inch long and about as wide as a kitchen match (exhibit 77).

EXHIBIT 75. Adult ♀ screwworm fly. Natural size, approximately:

EXHIBIT 76. Eggs of the screwworm fly attached to scab from a wound. About eight times natural size.

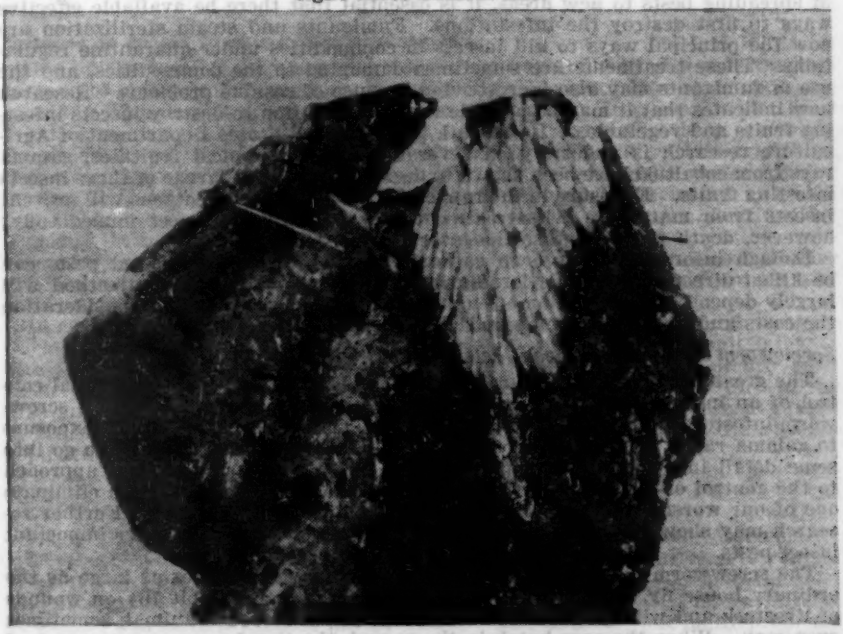
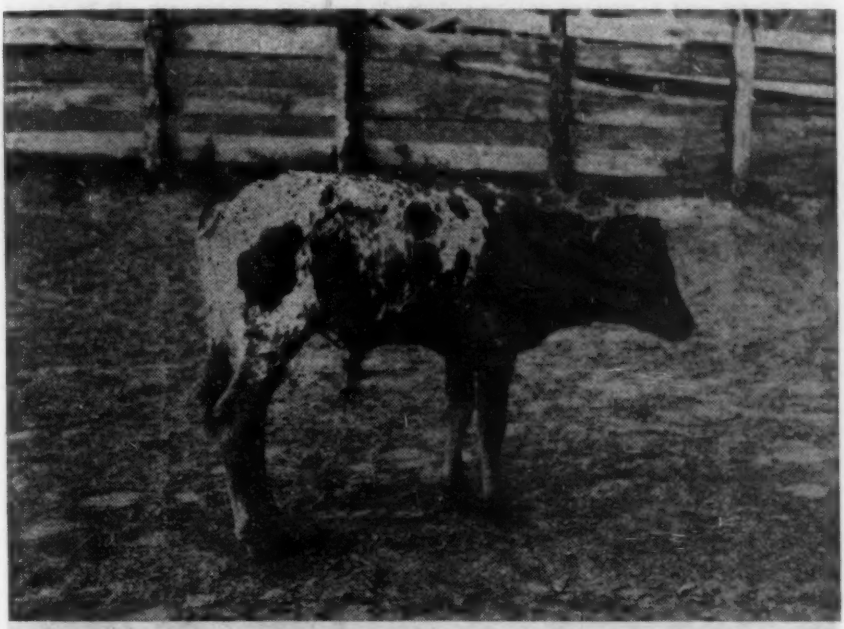


EXHIBIT 77. Larvae of the screwworm. Natural size approximately: ⊢—⊣

EXHIBIT 78. A severe screwworm infestation in steer. The infestation started on the ear where ticks were attached.



Each fly lays about 200 eggs in a wound. Maggots from this many eggs will cause severe destruction of tissues. However, the infested wound attracts more flies which give rise to more and more maggots. Within a few days to a week the infestation may contain several thousand maggots and the infested animal is literally eaten up (exhibit 78). Any wounded animal in heavily screwworm-infested areas is subject to attack. Once an infestation is started, and if untreated or uncared for, the animal will invariably be killed by the insect. When the maggots reach maturity they leave the animal and enter the ground where they pupate (exhibit 79). After about 10 days they are transformed into flies. The flies may migrate 25 miles or more in search for food and for wounded animals upon which they must develop.

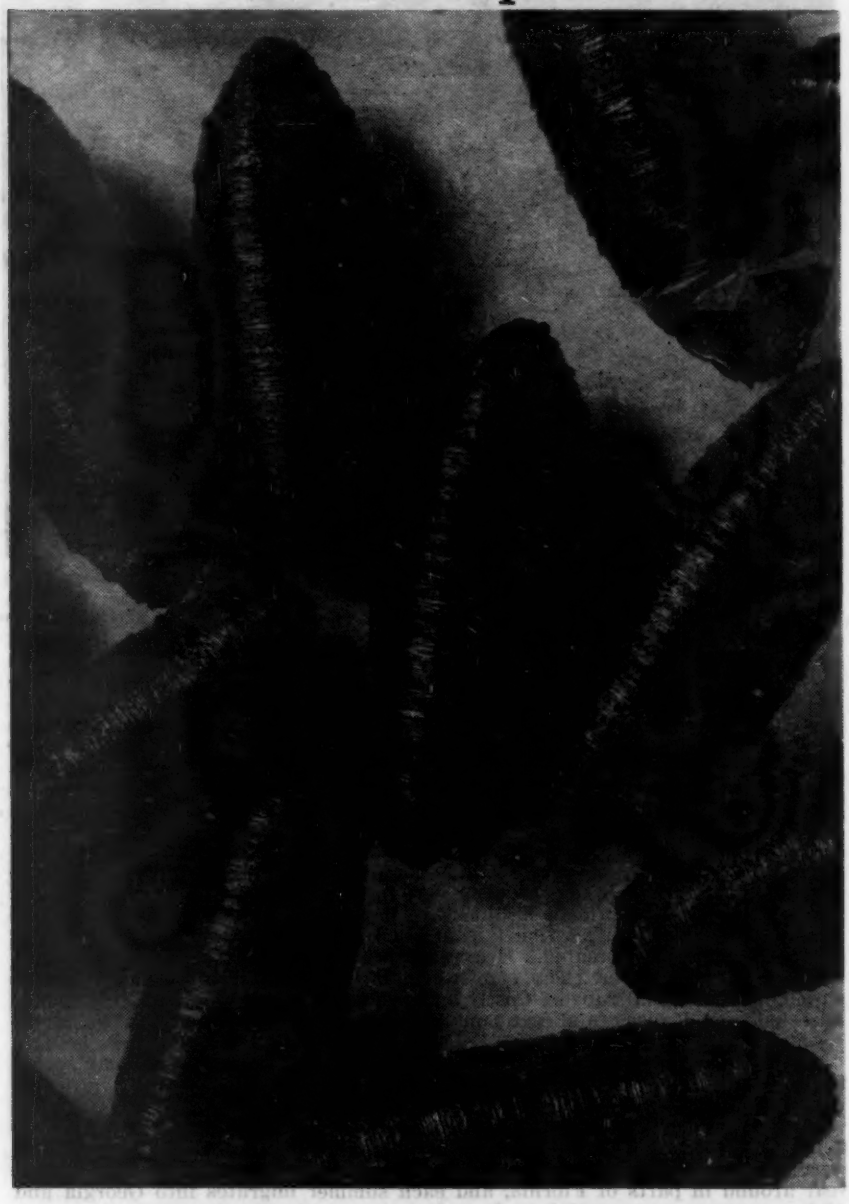
The screwworm is a native pest in Southwestern United States and greatest losses occur in that area. Stockmen in Texas, New Mexico, Arizona, and southern California each year spend millions of dollars for range riders to examine herds and treat wounds to prevent or cure infestations. In spite of these costly control measures, additional millions are lost because of animals that become weakened before an infestation is controlled or because of death losses among animals that are not treated. Heavy death losses also occur among game animals, particularly deer. The screwworm often becomes established in areas outside of its normal range. Costly outbreaks are not infrequent in Oklahoma, Missouri, and Kansas, and occasionally may occur as far north as Nebraska, Iowa, and South Dakota.

Fortunately winter weather kills out established infestations each year except in south Texas and the southern part of Arizona and California. The insect lives the year around in Mexico.

The screwworm did not exist in southeastern United States until 1933. In that year infestations became established in Florida when infested livestock were shipped into the area. It has been there ever since. It is destructive the year around in parts of Florida, and each summer migrates into Georgia and Alabama. In some years it spreads as far north as the Carolinas.

The annual cost of the insect to the livestock growers of the Southeast is conservatively estimated to average $10 million. Thus, since its establishment in 1933 the pest has cost the livestock industry in Florida, Alabama, Georgia, and the Carolinas at least $240 million.

EXHIBIT 79. Pupae (resting stage) of the screwworm fly. Natural size approximately: ⟊



For many years the stockman in this region sought for some way to eradicate the pest. The insect apparently cannot spread on its own from the Southwest to the Southeast. The area between south Texas and peninsular Florida is generally unfavorable for its winter survival and if the insect is not brought in with infested livestock there is every reason to believe that if eradication could be achieved, it would be permanent.

Among the methods considered for achieving eradication was that of liberating large numbers of sterile insects. Basic knowledge of the life history and the habits of the screwworm obtained through research supported this hypothesis. The normal population of the insect, even in heavily infested areas, is not very high. During winter months its range is greatly restricted and the population density is at a low point even in the overwintering areas. The insect can be raised in the laboratory in large numbers and at reasonable cost by using a mixture of ground beef and blood. Basic research years ago by geneticists and physicists and entomologists had demonstrated that X-ray irradiation at the proper stage in the development of certain insects causes sexual sterility without serious adverse effects on their behavior.

With this information, research was undertaken by several members of our staff to explore the possibility of utilizing sterile males of the screwworm as a means of its control. R. C. Bushland, D. E. Hopkins, A. H. Baumhover, A. W. Lindquist, A. J. Graham, and I are among the members of our staff who have developed this research project to the current state of knowledge. Excellent cooperation and assistance was obtained by several members of the Oak Ridge National Laboratory.

Exploratory research under laboratory conditions demonstrated these encouraging facts: (1) Exposure of screwworm pupae (the resting stage) to dosages of X-rays or gamma rays results in complete sterility of the flies that subsequently emerge from the pupae; (2) a dosage of about 3,000 roentgens causes sterility in males; about 4,000 causes sterility in females; (3) sexual behavior of irradiated insects is normal, so that the natural wild screwworms cannot discriminate between fertile and sterile screwworms in mating.

Tests were then conducted in laboratory cages to determine if the presence of sexually sterile males in a caged population of normal flies would reduce the reproductive capacity of the normal insects. Various ratios of sterile to fertile males were placed in cages with normal females and the percentage of sterile and fertile eggs produced by the females was determined. These studies showed that if sterile males equaled the number of normal fertile males almost one-half of the females produced infertile eggs. Similarly, if 80 percent of the caged males were sexually sterile about 76 percent of the females produced sterile eggs. The investigations showed also that female flies mated one time only and if they mated with a sexually sterile male, their biotic potential was destroyed. Tests indicated also that presence of sterile females in cages did not affect the final result.

These laboratory investigations indicated that the release of sufficient numbers of sexually sterile male flies among a natural screwworm population theoretically could result in greatly reduced reproductive potential of the wild insect population. The next step was to try this procedure in the field.

The first field trials were conducted during 1952 and 1953 on the 16-square-mile island of Sanibel off the west coast of Florida. The release of large numbers of sterile males caused a marked reduction in screwworm abundance indicating that the sterile males would compete fairly effectively with normal wild males in mating with wild fertile females. Complete eradication of the insect could not be demonstrated however, because normal flies from the Florida mainland 2 miles away and from nearby islands migrated onto Sanibel.

Since a valid test was not possible on a small scale in a large infested area such as south Florida, a cooperative agreement was reached with the Netherlands Antilles Government to attempt eradication on the small isolated and naturally infested West Indies island of Curaçao. This island has an area of 170 square miles. It is isolated from other infested areas by at least 40 miles. The screwworm fly population on the island was as high and perhaps much higher per square mile than that which occurs normally in Florida.

Research was initiated in March 1954. During the first 4 months scientists obtained information on the natural population density to aid them in estimating about how many sterile flies should be released to cause a downward trend in the natural population.

These studies led to the decision to attempt eradication by releasing each week about 400 sterile males per square mile. This rate of release, which would mean about 3 or 4 sterile males for each normal male, was to be maintained until eradication was achieved or until it was obvious that the method would not accomplish the objective.

Screwworms were reared at the Department's Orlando, Fla., laboratory; pupae were irradiated with 5,000 to 7,500 roentgens from a cobalt-60 source, and irradiated pupae were shipped by air to Curaçao. After the flies emerged

they were released over the island from small airplanes. Releases which started on August 9 were made 2 times each week at the rate of about 400 males per square mile per week. Sexually sterile females emerging from the irradiated pupae were also released because it is impractical to separate the sexes.

To measure results, goats were placed in 11 animal pens scattered over the island. The number of eggs deposited by flies and the percentage fertility of the eggs was determined during the course of the experiment. Reports were also received on the number of screwworm-infested animals which occurred among the livestock on the island.

Favorable results were quickly apparent. I have two charts which I would like to show at this point. The first (exhibit 80) gives figures which show how the sustained release of a preponderance of sterile males can theoretically eliminate an insect population in a short period of time.

EXHIBIT 80

Theoretical population decline when sterile males are added to a natural population

Natural population	Sterile males released	Ratio—sterile to fertile males	Population decline—theoretical maximum
1,000,000	2,000,000	2:1	333,333
333,333	2,000,000	6:1	46,619
46,619	2,000,000	42:1	1,107
1,107	2,000,000	18,000:1	Less than 1

In this example we are assuming an insect population in which biotic factors are causing the population to remain at a constant level. In this hypothetical case releases are started at the rate of two sterile males for every fertile male in the natural population. If we assume that the sterile males reduce the reproductive potential of the females to the maximum, the insect population will decline by two-thirds in the first generation. If such population reduction occurs and if the original release rate is continued, the ratio of sterile to fertile males will increase. This in turn will cause an even more rapid decline so that the second generation population will be correspondingly lower than the first. By the third generation the ratio of sterile to fertile insects will be so great that the chances of a female mating with a fertile male will be exceedingly slim. By the fourth generation, the odds against a fertile mating will be so great that we would not expect any insects to reproduce. To be certain, however, releases of sterile males should continue for several more generations.

I would like to emphasize that the figures given you are strictly theoretical; they do, however, explain the principle of population decline resulting from the release of sterile males in a stable insect population.

Now I would like to show you the data obtained in the screwworm eradication experiment conducted on Curaçao (exhibit 81). The first column shows the weeks after the start of the experiment. The second column shows the number of fertile egg masses collected on wounds of goats in the 11 goat pens. The third column shows the number of sterile egg masses collected from the goats. The fourth column shows the percentage of sterile egg masses.

EXHIBIT 81

Record of fertility of screwworm eggs and population decline after starting the release of sterile males on the Island of Curacao

Weeks	Egg mass record		
	Number of egg masses		Percent sterile
	Fertile	Sterile	
1	15	34	69
2	17	38	69
3	17	36	68
4	10	37	79
5	7	42	86
6	3	23	88
7	0	10	100
8	0	12	100
9	0	0	----------

You will note that sterile males mated with an average of about 70 percent of the wild females during the first 4 weeks. No decrease in population was apparent or expected during this period, which is about the maximum period for one generation of the insect. During the second 4 weeks, or the first complete generation of flies after releases of sterile males began, the percentage of sterile eggs increased considerably and a marked reduction in screwworm population is indicated. No eggs, either fertile or infertile, were collected on the 9th week. Thereafter, on the 14–15 weeks, 2 small infertile egg masses were collected. No further evidence of screwworm activity was noted on the island after this time. Livestock owners reported no cases of screwworms in livestock after the 9th week.

The release of sterile screwworm flies was discontinued in early January. At that time, within less than 5 months, it was concluded that complete eradication had been achieved. It is now about a year and a half since the experiment was concluded and no screwworms have been reported from Curaçao.

The Curaçao experiment proved the feasibility of the sterile male method for eliminating the screwworm from the Southeast. Research is now under way to develop practical procedures that can be applied in that area.

The elimination of the insect from the Southeast will be a huge and costly undertaking. The area in Florida in which screwworms normally overwinter comprises about 50,000 square miles. A program involving the release of 400 sterile males per square mile per week will necessitate the rearing and release of about 40 million screwworm flies per week. It might require 2 years of such intensive effort to accomplish eradication. Even so, the total cost of eradication would be less than the losses caused by the pest each year.

STERILE MALE TECHNIQUE FOR CONTROLLING OTHER INSECTS

In view of the success of the Curaçao experiment, there is increasing interest in research on this method of control for other destructive pests. It may prove successful againt a few. However, it is not likely that this approach will be widely applicable. Most insects occur in such great numbers that it would be impractical to rear, sterilize, and release enough insects to greatly reduce the normal population. Many insects cannot be reared in captivity or only at great cost. Other pests will not disperse widely enough to place sterile insects in a position to compete with the normal males. Some of our important pests reproduce without fertilization.

The fruitflies are one group of insect pests against which this method might be successful. Investigations are now underway in Hawaii to explore the possibility of eradicating incipient infestations of fruitflies, including the Mediterranean fruitfly which has recently become established in Florida. Scientists in Africa have expressed interest in the method as an aid in the control or elimination of the tsetse fly, one of the most damaging insects known. The method is worthy of exploratory investigation on a number of other important insects to determine if it will prove useful to supplement other control or eradication techniques.

To briefly summarize then, atomic energy has already proved a valuable entomological research tool and is potentially an important means of controlling certain insect pests. As our knowledge and our command of this energy source increases, we may find atomic energy to be one of our valuable insect-fighting weapons.

Dr. KNIPLING. Fine. Isotopes are proving very valuable in furthering our knowledge of the life history, habits, and biology of insects. They are proving valuable as tagged chemicals to study the mode of action of insecticides, to learn more about the toxicity of insecticides when fed to animals, so as to avoid the residue hazard, which is one of the chief obstacles to developing chemical control methods.

Ionized radiation has been investigated as a possible means of destroying insects directly in stored products, especially in grains, and work of this kind is under investigation. Insects can be destroyed in this manner, but engineering problems remain to be worked out to determine if the cost will compete with current methods of control and to be assured that no hazard will result from the use of the high intensity radiation facilities needed.

I believe the greatest advance that we have made in using atomic energy is in connection with the possible eradication of the screwworm, a very important insect pest of livestock in the southern parts of the United States.

The screwworm fly is an insect about three times the size of the housefly. It lays its eggs on wounds of animals, any warm-blooded animal, livestock in particular, and these eggs hatch and the maggots start feeding on the wounds.

I have some photographs here showing the different stages of the screwworm, the adults, the egg, the larvae, and the pupa stage, and also a photograph of an animal that is infested. When these eggs hatch on the wounds, the maggots start feeding and the wound becomes more attractive to more flies, more flies lay eggs, and you get multiple infestations.

In a matter of a week or 10 days, if the animal is not treated, it will literally be eaten up by the screwworm larvae. The stockmen in the Southwest in particular have spent millions of dollars every year, having range riders examine the animals to treat wounds to prevent infestation, or to destroy the infestation that might have started in the animal.

Senator BRICKER. How far north does it come? It doesn't get up into our country?

Dr. KNIPLING. It winters in the southern parts of Texas, Arizona, and California, and each spring it migrates northward probably on its own into Oklahoma and northern Texas, but through shipment of livestock it quite frequently gets established early in the spring in some of the northern areas.

It is not too uncommon to have outbreaks of the screwworm in Kansas, Nebraska, even in South Dakota, and in some of the other States, and whenever it becomes established early in the spring, it does a lot of destruction before winter.

However, in the wintertime, the cold weather kills it out to the southern part of the country again and the same process develops next year.

Representative PRICE. Warm weather——

Dr. KNIPLING. It is a warm-weather insect. It can't tolerate cold climates and exist year after year, but it does spread on its own from overwintering areas each summer.

The screwworm did not occur in the southeastern part of the United States until 1933. It became established in Florida in 1933.

Senator BRICKER. Where did they come from?

Dr. KNIPLING. They came from the Southwest, through shipment of infested animals. Infested animals were shipped into the Southeast and the infestation was started. Florida climate is suitable for overwintering of the screwworm and it has occurred in the Southeast ever since.

We estimated that the losses in the Southeast to the livestock industry amount to at least $10 million a year. Since 1933 the losses have amounted to perhaps 240 or 250 million dollars. The stockmen in the Southeast have been anxious to have some way of eliminating the screwworm from that area.

We feel that if it can be eradicated it can be prevented from reestablishing in the Southeast if infested animals are not shipped to the area. One of the methods that has been considered is the possibility of sterilizing male insects. I might say this screwworm can be reared in large numbers on a mixture of ground meat and blood in the laboratory and the number of insects in an area is never very great, in terms of many other insects, so we thought there was a possibility of sterilizing and releasing enough male screwworm flies in the area to achieve eradication. Research was therefore undertaken, first in the laboratory.

We had the cooperation of the Oak Ridge National Laboratory. They provided us with a cobalt-60 source to irradiate the insects. We found that when pupae of the screwworm fly are irradiated at the proper age with about 3,000 to 4,000 roentgens, the male flies, as they emerge later, are sterile, and also the females if they had up to 4,000 roentgens.

A series of laboratory investigations were undertaken to test the possibility in this way. For example, we would take a cage and have, say, 50 normal females and also 50 normal males, and we would add 50 sterile males to this population and see what percent of the normal females would then reproduce.

We found that these males that were irradiated would compete successfully with the normal males and mate with the females and roughly half of the females would produce sterile eggs, and if we increased that to 75 percent sterile males in the population, the number of females would produce roughly 75 percent sterile eggs, so tests were then run in the field to try to test the principle.

Investigations were conducted on Sanibel Island off the west coast of Florida and sterile insects were released and it was demonstrated that the released sterile males did compete fairly successfully with the normal wild males in mating with females on the island. A population decline was demonstrated, but we couldn't demonstrate eradication because flies from the mainland of Florida would fly over to the island even though it was 2 miles separated from the mainland. It was necessary to try to seek some small island, completely isolated island, where we could conduct a small-scale test.

Fortunately, we found an island that had a high population of screwworms. This was the island of Curaçao in the Netherland

Antilles. The Netherland Antilles Government was very willing to cooperate in running this experiment and we had their full assistance and cooperation in carrying out the investigations.

This island, by the way, is 170 square miles. It is 40 miles from the coast of Venezuela and we regard it as completely isolated and no opportunities for insects to come back in from other infested areas. The plan was to rear the screwworms in Florida, where the pupae were irradiated with the cobalt-60 source.

The pupae were shipped to the island of Curaçao and each week 400 sterile male screwworms were released per square mile. This continued over a period of several months. The flies were released by airplane. We had animals in some pens on the island to collect the eggs, to see what percent were sterile and to measure the number of eggs that were being deposited.

We had a record of the population density before the experiment started and by noting the number of egg masses we could determine the population decline. We could also determine the approximate decline by the number of animals that were being attacked by screwworms during the period.

I have two charts here that I would like to discuss. The first chart is strictly a theoretical picture. I want to show the principle that is involved.

Suppose we have an area in which there are a million normal male insects and we introduce regularly 2 million sterile males that are competing with the million fertile males. We will then have a ratio of 2 to 1, and the maximum theoretical decline in the progeny would be two-thirds.

In other words, you would only have one-third of the number the first generation after release of your sterile males. If that happens, and if you still continue to release the same number, in the second generation, you see, you will have a ratio of six sterile to every fertile male mating with the females in the population. That, in turn, will permit development of only one-seventh the original population.

Then you still continue to release this large number and then your ratio of sterile to fertile is 42 to 1, so your chances of mating with a fertile male are getting very, very slim and you have this proportion of decline. Then in the subsequent generation with still the same number, you have a ratio which is so great that you would expect complete elimination.

I want to emphasize that these figures are theoretical. They are just given you to show the principle involved under the most favorable circumstances.

I will show you the next chart, which will show you the results that we got on the island of Curaçao. This column shows the weeks after the experiment was started. In the second column are the number of egg masses that were collected on the animals in the 11 pens on the island, and this column shows the number of egg masses that were fertile and this shows the number that were sterile.

The last column shows the percentage of sterile eggs. I might say that in releasing 400 sterile males per square mile per week we estimated that the ratio of sterile males to fertile males on the island was roughly 3 or 4 to 1 when the releases were started. The results obtained are not too far from the theoretical in this case.

I might say that the life history of the screwworn is roughly 4 weeks, so you wouldn't expect any drastic effect the first 4 weeks. You will

note that the results are about the same during this period. We had roughly 69 percent of the screwworms which were producing sterile eggs.

This continued for the first 3 weeks at least. In the fourth week, which is near the beginning of the next generation, I think the results are beginning to show up. Drastic reductions are beginning to show here the fifth week, which is really the first full week in the second generation. The percentage of sterile eggs produced goes up. In the fifth week it had gone up to 86. In the sixth week it is essentially the same, but the total number of egg masses was reducing, showing that the population has declined.

By the seventh week the population had declined drastically, as indicated by the fewer egg masses, and there were so many sterile males in relation to the fertile ones that by our method of measuring we didn't get any fertile eggs here during this period. We had 100 percent sterile of those that were collected.

I don't show it down the line, but after the ninth week we didn't get any fertile eggs. About the 12th or 14th week we got 2 egg masses and both were sterile. We continued to release flies at the rate of 400 flies per square mile per week until about the fifth month, just to be sure that if there were any fertile flies on the island they would be exposed to these sterile males, and thus the opportunity of mating with a few fertile males would be negligible. No screwworn cases were noted in animals after the ninth week.

By January, the fifth month after the start of the experiment, the experiment was terminated with the conclusion that the screwworn had been eradicated from the island.

It has been a year and a half now since the experiment was terminated and they have not recorded any screwworms on this small island.

Senator BRICKER. How quickly is the program in Florida going to start? Have you started the operation there yet?

Dr. KNIPLING. We are now in the stage of research to adapt the methods from this small scale to a large scale. We are strictly still in the research phase. We feel that in about a year we will have completed all of the necessary research and will have developed ways and means of rearing the insects in the tremendous numbers that would be required to try to eliminate the screwworm from the Southeast.

We would be going from an island of 170 square miles to an area of 50,000 square miles in trying to eliminate the screwworm from Florida. According to our estimates, on the same basis as on Curaçao, 40 million screwworm flies per week will have to be released. We feel the program should be continued for a period of 2 years.

Theoretically, if the trend follows the same course as on Curaçao, it would all be over in 6 months, but we would not want to recommend a program for less than 2 years.

Senator BRICKER. In the meantime, the infestation is treated medically?

Dr. KNIPLING. Yes. In the meantime the stockmen are watching their animals and if they find infested animals they treat them with the methods that are now used and they watch the animals until the wound heals.

An animal is not subject to attack unless it has some sort of wound.

Representative VAN ZANDT. How does the screwworm function?

Dr. KNIPLING. The fly lays eggs on the wound of the animal, any break in the skin, and these eggs hatch in the maggots and these maggots actually feed on the living tissues. More flies lay more eggs and you may get three or four thousand of these maggots in the animal. They will just practically eat the animal alive, like the picture you have there of the steer that shows the infestation in the head.

It would just be a matter of a day or two after that and if it wasn't treated this animal would be killed as a result of that infestation. Our people working on this problem are fully confident that we can eliminate the screwworm from the Southeast in this manner.

It will be a costly undertaking. We feel that the cost would be several million dollars to complete the job. We estimate that losses are at least $10 million a year and we think it would be certainly a good long-term investment if we could eliminate it by this means.

Senator BRICKER. How was this worm brought into the Southwest?

Dr. KNIPLING. It is native all through South and Central America and south Texas. It is a native insect.

Representative VAN ZANDT. Does it have any useful purpose?

Dr. KNIPLING. No useful purpose at all. It is very destructive. It is probably the most important livestock pest in the area in which it occurs.

Representative VAN ZANDT. Do birds use it for food?

Dr. KNIPLING. No. They might, but it certainly would not be an important item in any animal's diet. In the first place, the number of insects present are relatively small compared to other insects.

Representative VAN ZANDT. How long does it take to sterilize the males?

Dr. KNIPLING. Well, the pupae—that's the resting stage—are exposed in a cobalt-60 source. It probably takes about 15 minutes or so to get the 3,000 roentgens that are required to sterilize. You have to sterilize the pupae at the right stage. If you sterilize too early you do too much damage to the insect and you will kill it, or if you don't kill it it will still be fertile.

The radiation has to take place at the proper stage of development of the cells in the male sex organs.

Representative PRICE. Have you done this work on any other type of insect as, for instance, the Mediterranean fruitfly that you read about?

Dr. KNIPLING. Yes. We are very much interested in the possibility of utilizing this technique for controlling a few other important insects. We are certain that it will not work on most insects. There are just too many insects in existence of certain kinds so that it would be impossible to raise and release enough insects to affect the population. However, we are very much interested in a number of these and the Mediterranean fruitfly is one of them.

Representative PRICE. Are you working on the Mediterranean fruitfly?

Dr. KNIPLING. We are doing some work in Hawaii now. We are just investigating the possibilities, and we have found that the same principle so far as sterilizing the insect holds. These insects mate more frequently than the screwworm, but we still have this possibility of releasing sterile insects in sufficient quantities to effect a downward trend in the insect population.

However, the work is not advanced far enough where we would want to consider this procedure in connection with efforts to eliminate the Mediterranean fruitfly outbreak now. We are using other methods, but we think it shows possibilities for new or light infestations of fruitflies, not only the Mediterranean, but several others.

Representative VAN ZANDT. Doctor, what about the facilities to do this job in Florida? Will the existing facilities be adequate or will you have to build new ones?

Dr. KNIPLING. So far as our research is concerned, we feel that we have adequate facilities to complete the job. If they go into an actual eradication program it will take a lot of facilities. It will take larger radiation sources to do the job rapidly. It will take a huge insect-rearing plant and all the facilities that go with it, and of course a lot of manpower.

Representative PRICE. How would you keep it up? You eradicate for a few years, or——

Dr. KNIPLING. It would be necessary to examine livestock that are shipped into the Southeast to be sure that they are not carrying any infestation with them.

Representative VAN ZANDT. With regard to the figure of $3 million you mentioned a moment ago, will that figure include the cost of construction of sufficient facilities to do the job?

Dr. KNIPLING. If I mentioned $3 million I didn't intend to be specific. I believe I said several million. Actually, the best estimate now is that the total cost of eradication over a 2-year period, including all of thefacilities and so on, will probably be in the order of 5 or 6 million dollars.

Representative PRICE. Doctor, I am awfully sorry, but both Mr. Van Zandt and I are members of the House Armed Services Committee and we have bills on the Consent Calendar and I have to leave and Mr. Van Zandt has 1 or 2 of them.

Certainly I think we got the main point of your testimony. If there is anything else briefly you think you ought to call our attention to, I would appreciate it if you would do that, but we have to close here.

Dr. KNIPLING. I don't know if you are interested or not. I just happened to bring this along. That shows you the appreciation of the Netherlands Antilles Government for the job that was done by our people there.

Representative PRICE. Is this an award to you?

Dr. KNIPLING. No. It was awarded to the team that did the work.

Representative PRICE. To the team itself?

Dr. KNIPLING. That is right. [Reading:]

The Government of the Netherlands Antilles does tender by these presents its best thanks to the United States Department of Agriculture, Washington, D. C., United States of America, for promoting and carrying out in 1954 Operation Screwworm, a project to eradicate the screwworm in Curaçao, and kindly requests said Department of Agriculture to extend the expression of its gratitude to all these who actually contributed in the performance of a splendid job, in particular to—

Mr. B. T. Shaw and Dr. A. W. Lindquist for promoting the project;

Messrs. A. H. Baumhover and W. D. New, project leader and aid, for their performances in the field;

Messrs. A. J. Graham, D. E. Hopkins, and H. R. Dudley for their laboratory work of rearing and radiating the flies.

A. A. M. STRUYKKEN,
Governor of the Netherland Antilles.

Representative PRICE. That indicates that was an effective job in that particular island, and evidently worked very successfully and should cause some degree of optimism for an attack on the problem in Florida successfully.

It is a very interesting project. It is certainly one that shows very conclusive evidence of what you can do with radiation. Certainly it would be a great contribution in itself on the part of the atomic energy program for the livestock industry, and many other contributions that the program makes.

Thank you very much, Doctor, and thank you, Dr. Dunham. We are sorry that we have to rush away like this.

Dr. DUNHAM. I understand.

Representative PRICE. It is necessary.

I particularly have to be there because I am in charge of three of the bills and I have to follow them.

The committee then will adjourn until tomorrow morning at 10 a. m. We will meet again in the same chamber.

Thank you.

(Whereupon, at 12:15 p. m., Tuesday, June 5, 1956, the subcommittee recessed, to reconvene at 10 a. m., Wednesday, June 6, 1956.)

PROGRESS REPORT ON RESEARCH IN MEDICINE, BIOLOGY, AGRICULTURE, AND FOOD PRESERVATION

WEDNESDAY, JUNE 6, 1956

CONGRESS OF THE UNITED STATES,
SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT,
JOINT COMMITTEE ON ATOMIC ENERGY,
Washington, D. C.

The subcommittee met at 10 a. m., pursuant to recess, in room P–63, the Capitol, Representative Melvin Price (chairman of the subcommittee) presiding.

Present: Senators Pastore and Bricker; Representatives Price and Van Zandt.

Representative PRICE. The committee will be in order. This will be a continuation of the hearing to receive progress reports on the use of atomic energy in the field of medicine today. Dr. Dunham, will you continue as you did yesterday? I see that you have Dr. Sweet beside you. I had the pleasure of being in his company 2 years ago at Brookhaven.

Dr. SWEET. That is right, sir.

STATEMENT OF DR. C. L. DUNHAM, DIRECTOR, DIVISION OF BIOLOGY AND MEDICINE, UNITED STATES ATOMIC ENERGY COMMISSION

Dr. DUNHAM. Mr. Chairman, the first medical scientist to report is Dr. William Herbert Sweet, associate clinical professor of surgery, Harvard Medical School, Boston. He is going to report on the use of radioisotopes in the diagnosis of brain tumors.

Representative PRICE. That is a very interesting subject to this committee, Dr. Sweet, because quite a few of us took that trip to Brookhaven, and saw at first hand what you were doing and hoping to do in this field. Will you proceed with your statement.

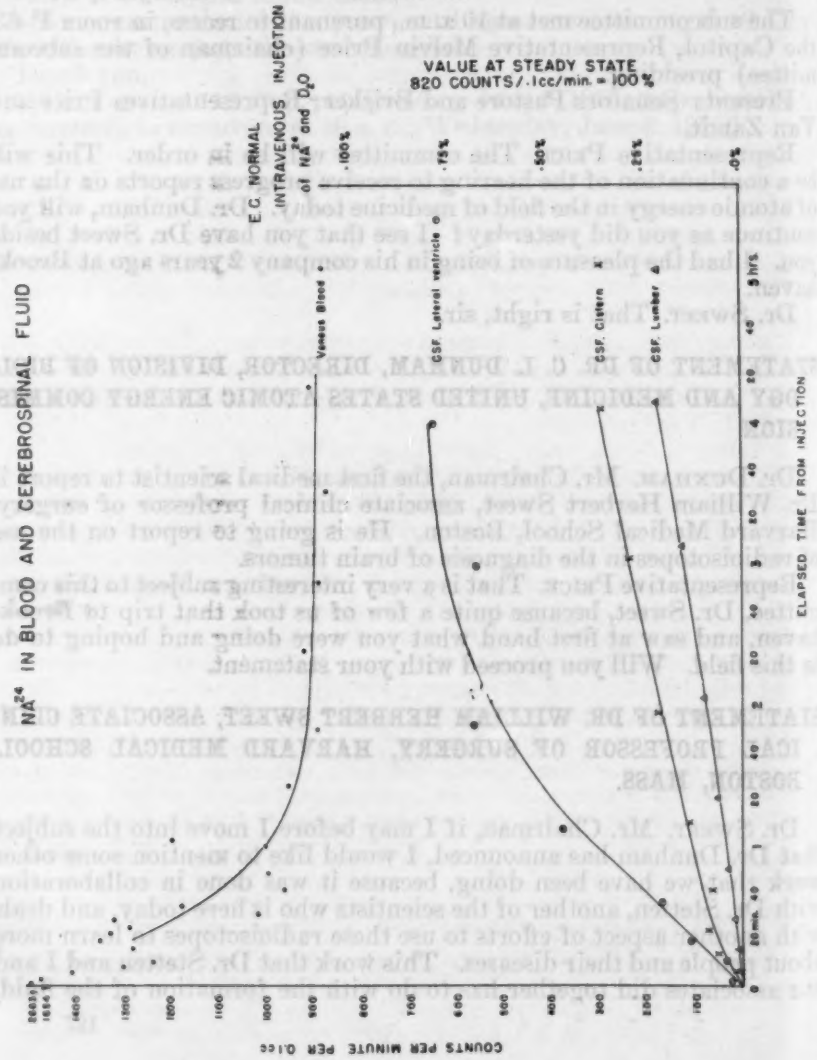
STATEMENT OF DR. WILLIAM HERBERT SWEET, ASSOCIATE CLINICAL PROFESSOR OF SURGERY, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

Dr. SWEET. Mr. Chairman, if I may before I move into the subject that Dr. Dunham has announced, I would like to mention some other work that we have been doing, because it was done in collaboration with Dr. Stetten, another of the scientists who is here today, and deals with another aspect of efforts to use these radioisotopes to learn more about people and their diseases. This work that Dr. Stetten and I and our associates did together has to do with the formation of the fluid,

called cerebrospinal fluid, which is within and around the surface of the brain and spinal cord. This is a pretty important fluid because in some way it is associated with the terrific swelling of the brain that sometimes occurs, especially when we try to operate on the brain.

The old idea about this fluid was that all of it was formed in the center of the brain. Exhibit 82 is an indication of some data obtained from a patient following the intravenous injection of a labeled substance, the radioisotope of sodium. One sees that this substance entered rapidly from the blood into the fluid-containing cavity in the center of the brain, the ventricle, whereas it has entered much more slowly into the spaces outside the brain. From these data we thought we had confirmed the old idea that this fluid is formed in the center of the brain and flows out from there onto the surfaces.

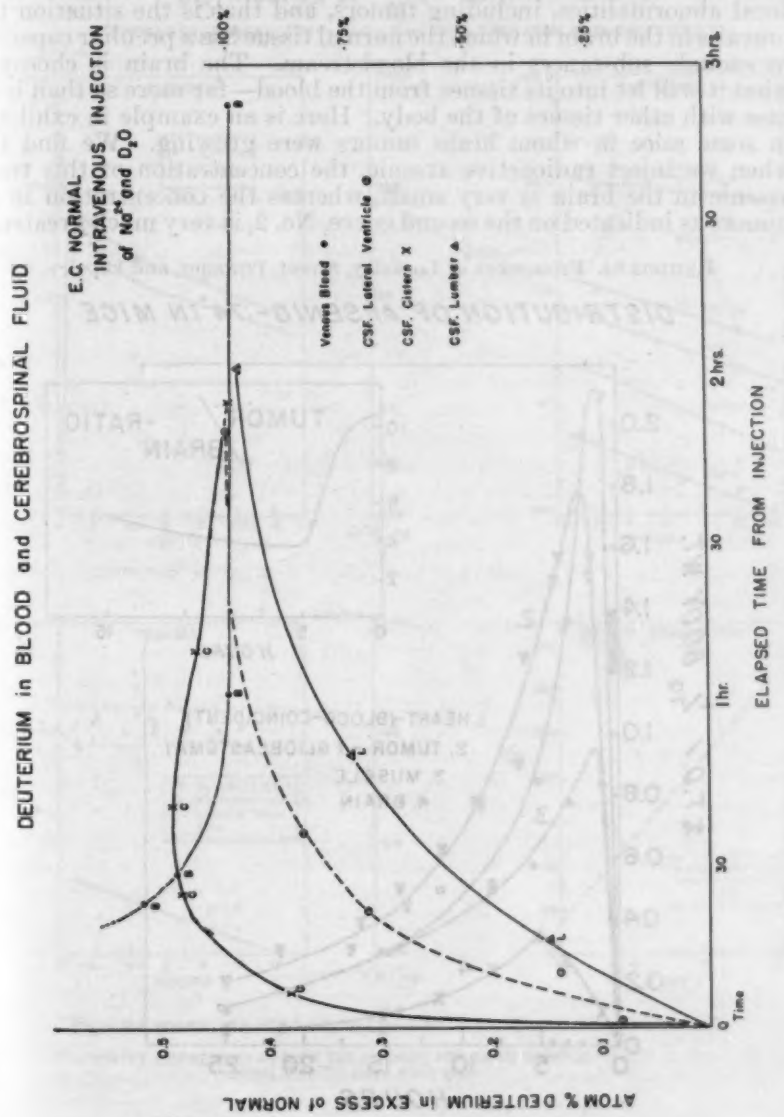
EXHIBIT 82



But when we went ahead to the work that Dr. Stetten and I did together, the results of which are shown in Exhibit 83, we found that labeled water—heavy water—entered much more slowly into the cavity that is in the center of the brain, the ventricle, than it did into the space outside the brain, called the cisterna magna.

So we had this evidence that the labeled water actually enters an area on the surface of the brain faster than it does one of these cavities

EXHIBIT 83

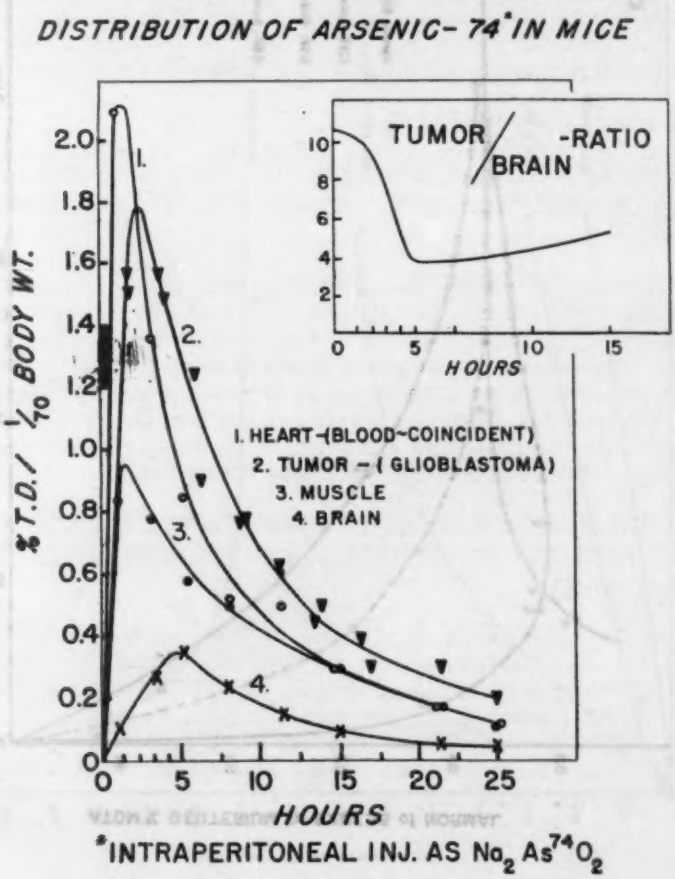


in the center of this organ. We have followed up this observation since then in an effort to understand a plaguing problem we surgeons have in the treatment of swelling or edema of the brain. This may not only occur following operations but may also be a bad problem after head injuries.

I shall pass on from this subject to my announced topic, the localization of tumors. You are probably familiar with the fact that certain special tumors, those of the thyroid gland, have a peculiar affinity for iodine. Such eagerness on the part of the tumor cells to take up a particular radioisotope is, however, unusual.

But there is another helpful mechanism that enables us to diagnose focal abnormalities, including tumors, and that is the situation that prevails in the brain in which the normal tissue has a peculiar capacity to exclude substances in the bloodstream. The brain is choosy of what it will let into its tissues from the blood—far more so than is the case with other tissues of the body. Here is an example in exhibit 84 in some mice in whom brain tumors were growing. We find that when we inject radioactive arsenic, the concentration of this tracer arsenic in the brain is very small, whereas the concentration in the tumors as indicated on the second curve, No. 2, is very much greater.

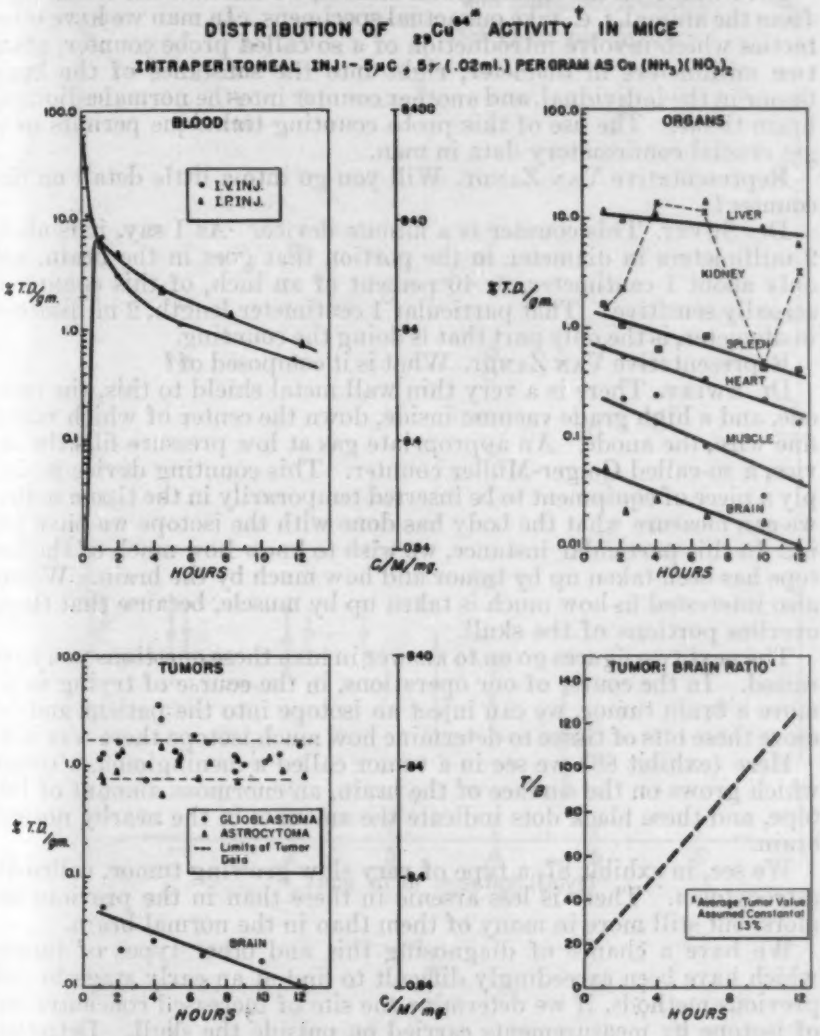
EXHIBIT 84. From work of Locksley, Sweet, Powsner, and Lepoire.



If we abstract from these data the information in which we are particularly interested, the ratio between the amount of the isotope in the tumor and that in the brain, we see in these mice for the first few hours after injection a much higher level in the tumors than in the brain.

A similar state is illustrated in Exhibit 85, showing what happened when we tried in our mice a radioisotope of copper. I draw your attention to the steady rise for several hours in the ratio of the concentration in tumor to that in the normal brain.

EXHIBIT 85. From work of Locksley, Sweet, Powsner and Lepoire.



* $T_{1/2}$ = 12.8 HOURS.; 19% β^+ – 0.66; 39% β – 0.57; γ – 1.35

† ACTIVITY EXPRESSED AS % OF TOTAL DOSE PER GRAM SAMPLE. NORMALIZED TO 25 gm. BODY WT.

This reaches a ratio of over 100 to 1, or 10,000 percent. One also notes that a number of normal tissues, such as liver and kidney, take up amounts of copper even greater than those found in the tumor. The high ratios tumor: brain occur principally because the brain permits so little to enter it.

Representative VAN ZANDT. What was the material you mentioned?

Dr. SWEET. This is copper that was used in this particular instance.

Senator PASTORE. Doctor, how do you follow the travel of the isotope?

Dr. SWEET. In the experimental animal, we can take the tissue right from the animal, i. e., take out actual specimens. In man we have other tactics which involve introduction of a so-called probe counter, about two millimeters in diameter, right into the substance of the brain tumor in the individual, and another counter into the normal adjoining brain tissue. The use of this probe counting technique permits us to get crucial confirmatory data in man.

Representative VAN ZANDT. Will you go into a little detail on this counter?

Dr. SWEET. This counter is a minute device. As I say, it is about 2 millimeters in diameter in the portion that goes in the brain, and only about 1 centimeter, or 40 percent of an inch, of this counter is actually sensitive. That particular 1 centimeter length, 2 millimeters in diameter, is the only part that is doing the counting.

Representative VAN ZANDT. What is it composed of?

Dr. SWEET. There is a very thin wall metal shield to this, the cathode, and a high grade vacuum inside, down the center of which runs a fine wire, the anode. An appropriate gas at low pressure fills the device, a so-called Geiger-Müller counter. This counting device is simply a piece of equipment to be inserted temporarily in the tissue so that we can measure what the body has done with the isotope we have put in. In this particular instance, we wish to know how much of the isotope has been taken up by tumor and how much by the brain. We are also interested in how much is taken up by muscle, because that tissue overlies portions of the skull.

The next two figures go on to answer in man these questions you have raised. In the course of our operations, in the course of trying to remove a brain tumor, we can inject an isotope into the patient and remove these bits of tissue to determine how much isotope there was in it.

Here (exhibit 86) we see in a tumor called a meningioma, a tumor which grows on the surface of the brain, an enormous amount of isotope, and these black dots indicate the amounts in the nearby normal brain.

We see, in exhibit 87, a type of very slow growing tumor, called an astrocytoma. There is less arsenic in these than in the previous tumors, but still more in many of them than in the normal brain.

We have a chance of diagnosing this and other types of tumor, which have been exceedingly difficult to find at an early stage by our previous methods, if we determine the site of increased concentration of isotope by measurements carried on outside the skull. Detection of the tumor with apparatus outside the intact skull requires the use of isotopes which give rise to gamma rays, since only such radiation will penetrate the bone. Our task is to spot a small, concentrated source of gamma rays amidst a larger area of tissue, the brain, which

EXHIBIT 86. Radioactive Assays As^{74}, Human Tissue Sample of Normal Brain and Brain Tumor (meningioma).

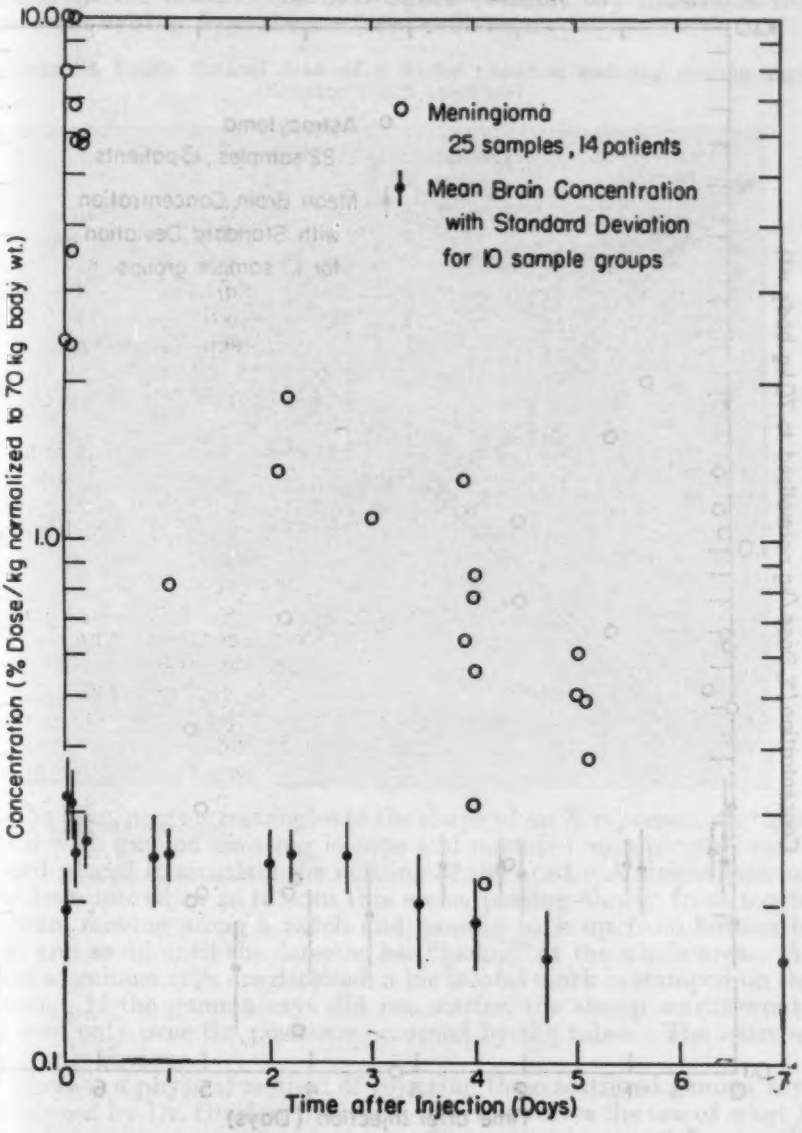
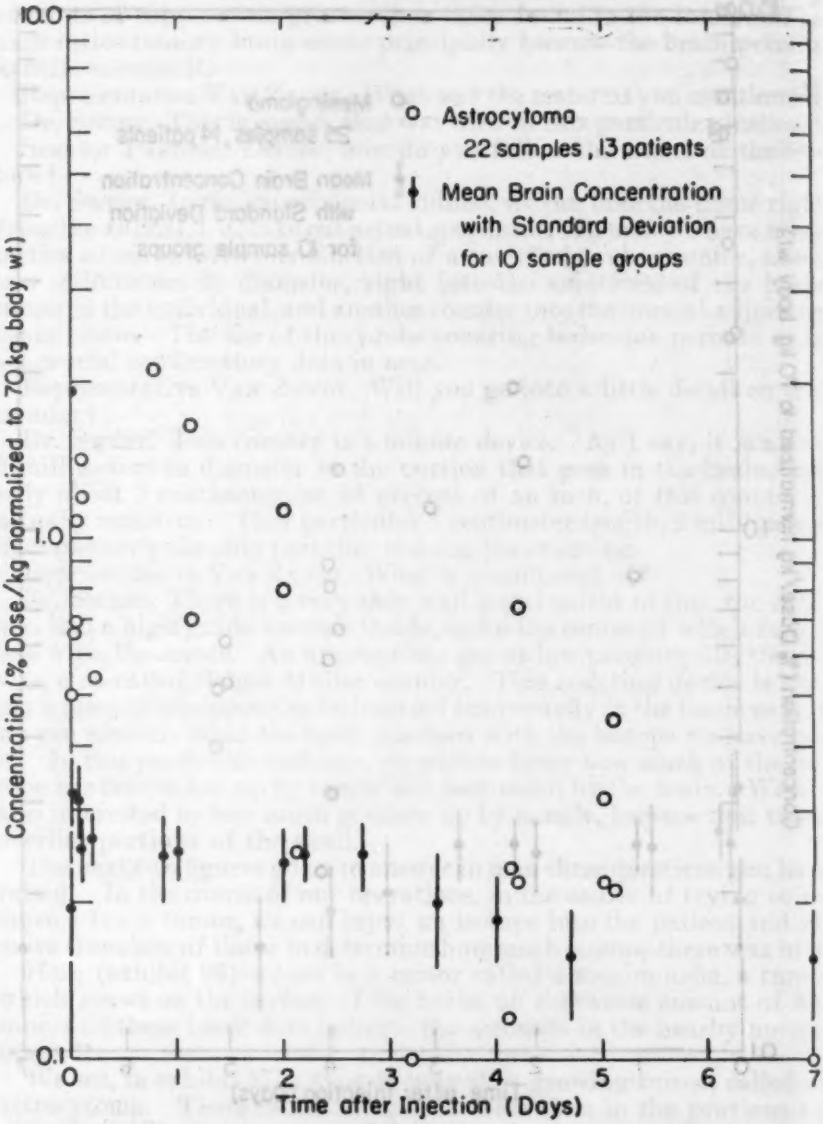


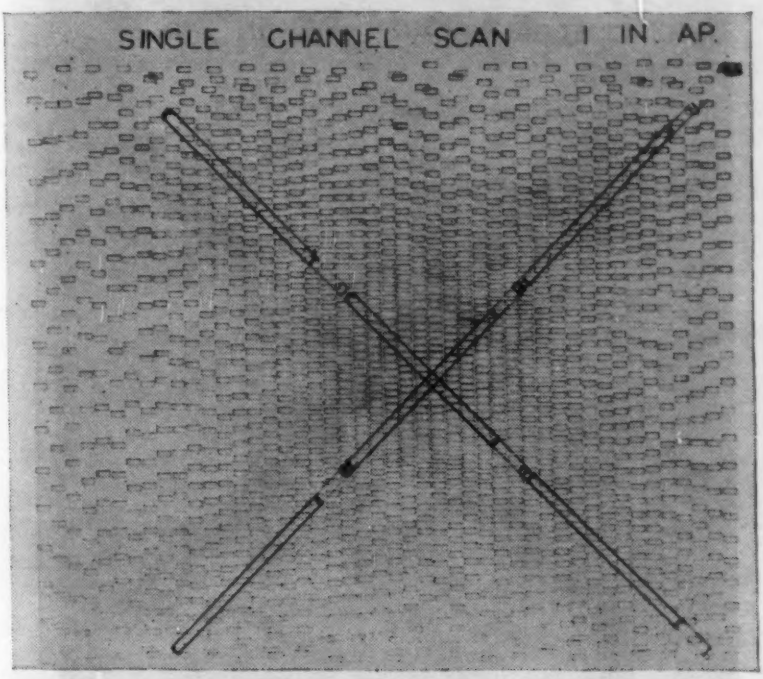
EXHIBIT 87. Radioactive Assays As^{74}, Human Tissue Samples of Normal Brain and Brain Tumor (astrocytoma)



is giving rise to lesser numbers of gamma rays. Unhappily, these rays do not continue to travel in straight lines in tissue, but bounce off in a new direction whenever they strike other particles of atoms. If all of the scattered as well as the undeflected gamma rays are counted, there emerges at the surface of the skull an enlarged, blurred image of the tumor within, and, if the tumor is small or contains but

little extra isotope, the image may get lost in the background of radiation from the brain. The next figure (exhibit 88) illustrates the confusion arising from the scattered radiation.

EXHIBIT 88. Single channel scan of a 6-tube phantom emitting gamma rays (detector 1-inch aperture).

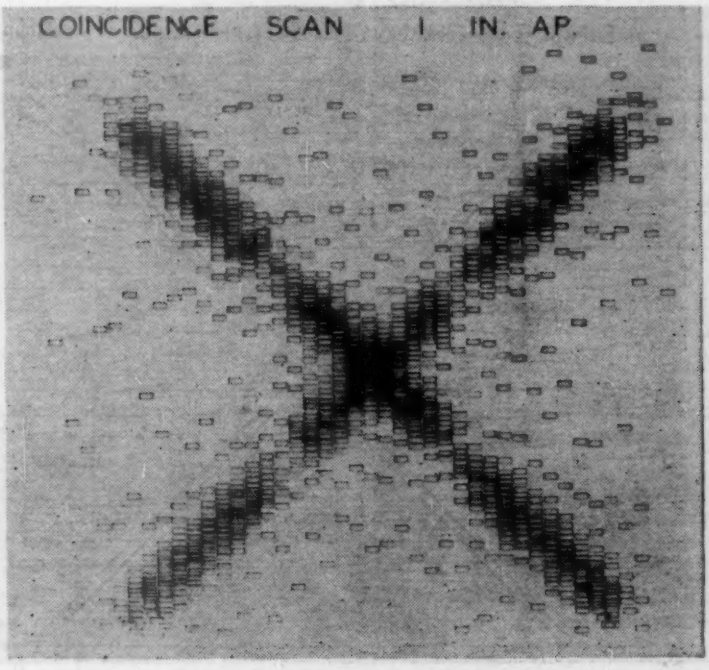


The long, narrow rectangles in the shape of an X represent six tubes filled with gamma emitting isotope and mounted on a piece of cardboard placed to simulate the midline of the head. A single detector has been moved so as to scan this scene, passing slowly from top to bottom, moving along a notch and passing back up from bottom to top, and so on until the detector has "looked" at the whole area. As soon as gamma rays are detected, a horizontal mark is stamped on the paper. If the gamma rays did not scatter, the stamp marks would be seen only over the positions occupied by the tubes. The extreme scatter is obvious.

There is a physical method of rejecting these scattered gamma rays developed by Dr. Gordon Brownell, which involves the use of what is called a positron-emitting isotope. These positive particles are the same size as the far more numerous electrons, which are negatively charged particles. A positron given off at nuclear disintegration soon collides with an electron to give rise to a pair of gamma rays, which leave the scene of the collision in opposite directions to each other. By using a pair of detectors, one on each side of the head, we can arrange the electronic circuits therefrom so that scattered gamma

rays are not counted. In exhibit 89 we illustrate the more accurate picture of the six tubes which ensues when this refinement is used to eliminate the scattered rays from the recorded count.

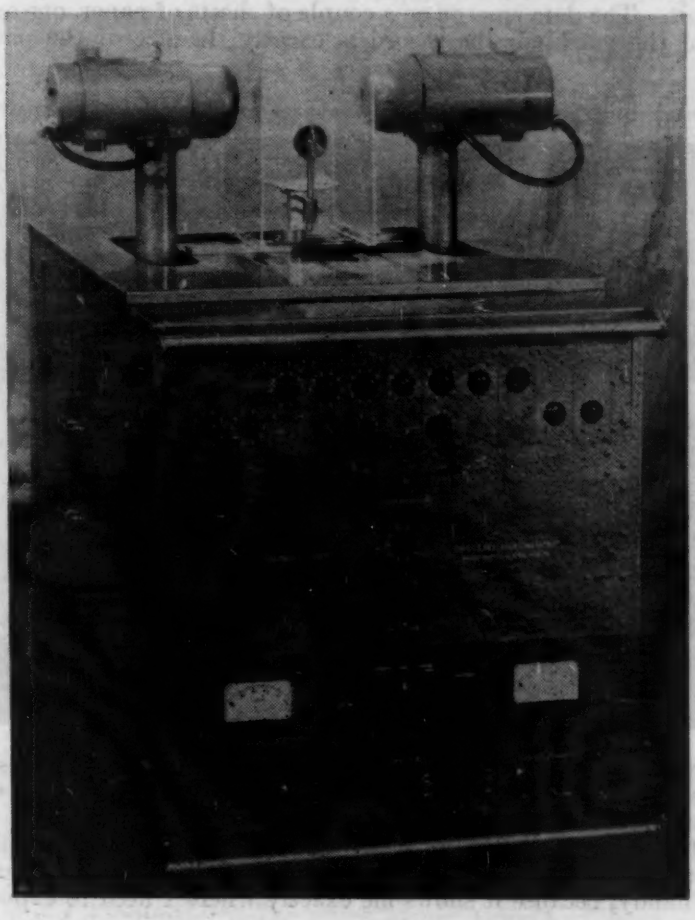
EXHIBIT 89. Coincidence scan of a 6-tube phantom emitting gamma rays (detector 1-inch aperture).



Because of this major advantage of a positron-emitting isotope, we have searched largely in this group for a substance which would localize in brain tumors. Of the two elements I mentioned earlier, arsenic and copper, both have useful positron-emitting isotopes.

Exhibit 90 shows the apparatus that has been used to count the paired gamma rays arising from the positron-electron collision. Two counting devices are involved, one on each side. The patient's head lies between them, and the mechanical and electronic units are contained in the cabinet below.

EXHIBIT 90. The automatic scanning coincidence counting apparatus.



In the next figure (exhibit 91) we see the relation of the patient to the unit. The data emerge on a couple of sheets of paper, one on each side of the machine; the record is exactly the size of the patient's head.

EXHIBIT 91. The automatic scanning apparatus in relation to the patient.

In exhibit 92 we illustrate a normal scan. The increased density of marks in the lower part of the side view of the head is due to the increased uptake of isotope in the muscles lying in this region. Contrast this with exhibit 93, in which the zone of increased isotopic uptake indicates the site of tumor. This to me as a surgeon is exceedingly handy, because it shows me exactly where I need to expose the brain.

Representative PRICE. Doctor, the machine you showed on the previous slide, is that in use?

Dr. SWEET. Yes. That has been in use for over a year.

Representative PRICE. Is that in any way taking the place of the use of the large reactor at Brookhaven for such a purpose?

Dr. SWEET. This is just for diagnosis. All this does is tell us, in what is often as you see a precise way, exactly where a tumor is. It does nothing about treating the tumor, but is purely for diagnosis.

Representative PRICE. The treatments are still being made on top of the reactor at Brookhaven?

Dr. SWEET. Yes, sir. I might mention that this apparatus has another feature. I said there was another piece of paper on the other side on which data are recorded. All the scan of figure 12 tells us is the localization of the tumor in two dimensions; the side and depth of the mass are not indicated. These additional data appear in another form of scan which is recorded simultaneously and which tells us the degree of asymmetry of the total gamma radiation—that is

EXHIBIT 92. Normal scan of coincidence counts—(positrocephalogram).

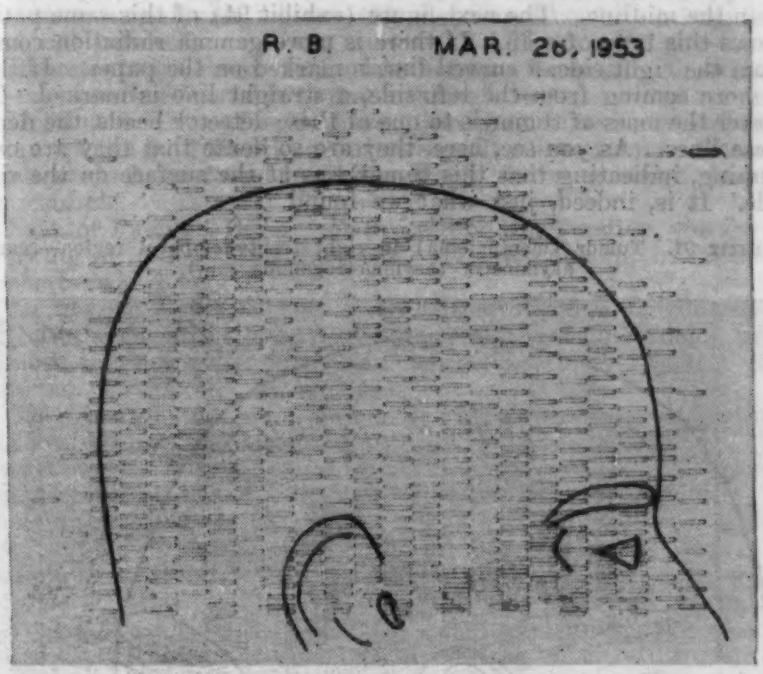
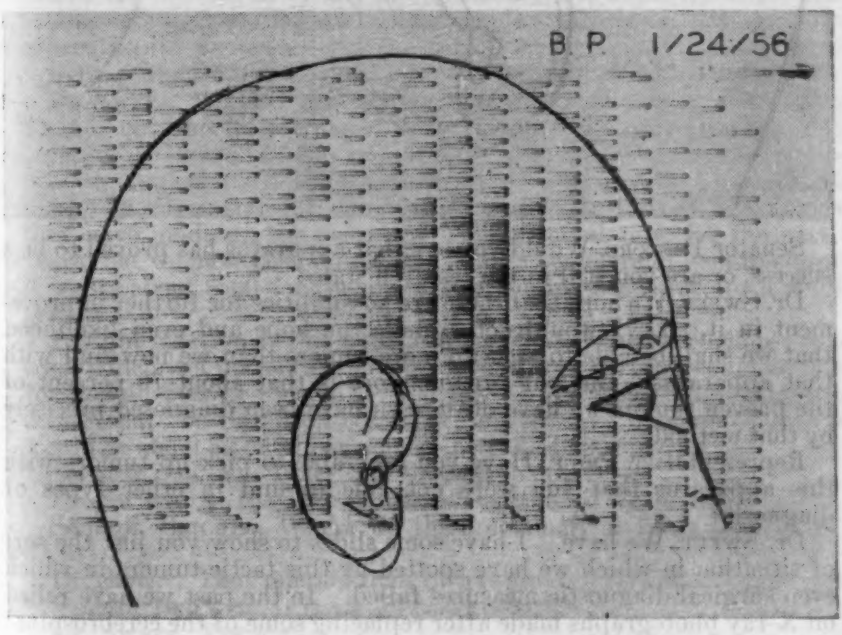
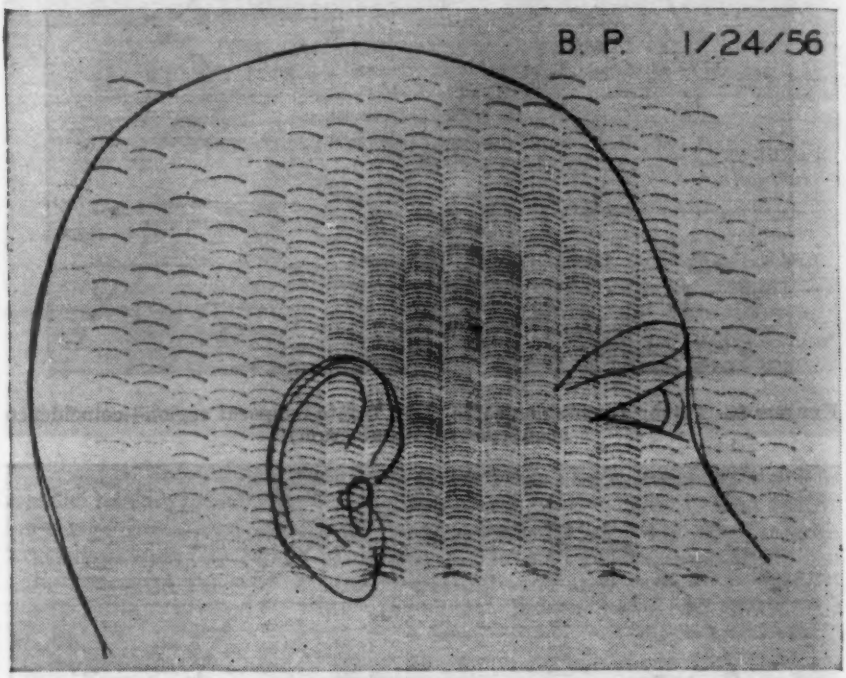


EXHIBIT 93. Tumor (meningioma) in right fronto-temporal region—coincidence scan (positrocephalogram).



to say, whether the abnormal area is on the right side, the left side or in the midline. The next figure (exhibit 94) of this same patient shows this type of scan. If there is more gamma radiation coming from the right side, a curved line is marked on the paper. If there is more coming from the left side, a straight line is marked. The nearer the mass of tumor is to one of these detector heads, the denser these lines. As you see, here, they are so dense that they are overlapping, indicating that this tumor was at the surface on the right side. It is, indeed, just what we found.

EXHIBIT 94. Tumor (meningioma) in right fronto-temporal region—scan of asymmetry (asymmetrogammagram).



Senator PASTORE. Would you say that apparatus has proved to be a success, or are you still in the research state?

Dr. SWEET. We hope that there are possibilities for further improvement in it, sir. I would not exclude the hope and even likelihood that we shall be able to pick up more tumors than we now find with that apparatus. But our present score is that about 70 percent of the proven tumors we have dealt with have been diagnosed precisely by that method.

Representative PRICE. Have you been able to pick up tumors with this apparatus that you were not able to find in other types of diagnosis?

Dr. SWEET. We have. I have some slides to show you just the sort of situation in which we have spotted by this tactic tumors in which even surgical diagnostic measures failed. In the past we have relied on X-ray photographs made after replacing some of the cerebrospinal fluid by air or taken during injection of a radio-opaque liquid into

arteries going to the brain. These maneuvers are somewhat painful and carry a small risk, whereas this scanning procedure is both harmless and painless.

Representative PRICE. You mean that sometimes after these special X-rays you were not able to find a tumor?

Dr. SWEET. Even after we have injected air into the cranial cavity or an opaque fluid into the arteries, we still missed tumors after those studies which we found by this method. I was going to show you an example.

Senator PASTORE. Before you proceed on this question, you say it is working in 70 percent of the cases. How do you explain the 30 percent where it has not?

Dr. SWEET. There are two general situations in which this method fails. In one, there is an exceedingly slow-growing tumor that is almost, but not quite, inert, and hence takes up very little of the isotope.

Then there is another situation in which a small tumor blocks the outflow of this cerebrospinal fluid to which I alluded earlier. When that occurs the fluid is dammed back, and behaves as a growing tumor. It accumulates and causes destructive pressure on the brain, even though the actual tumor is tiny. As a matter of fact, the air injection method tends to pick up tumors of that kind, whereas it is likely to miss tumors that are fairly near the surface of the brain, and can on that account be rather readily removed. Especially if they are spotted at an early stage, which this radioactive scanning method seems to enable us to do, we have a good chance of treating effectively tumors near the surface of the cerebral hemisphere.

So these methods are in a sense complementary. Ours has not replaced the old tactics by any means completely, but it has enabled us to diagnose tumors that are in a favorable group from the standpoint of treatment.

Representative VAN ZANDT. How widely is this machine used?

Dr. SWEET. We have the only machine which is actually in use today. That is not because the machine is difficult to obtain or make. It is because of the lack of the appropriate isotope, the positron-emitting isotope of arsenic. This has to be made in a cyclotron. Through our happy arrangement with the Massachusetts Institute of Technology, they have made up the necessary isotope for us now for the past 3 years that we have been doing this. But a commercial firm to supply it wants about $200 for the amount of isotope necessary for a single person.

I might mention at this point the fact that if the Oak Ridge cyclotron, which is a powerful one with a very high current, could be used for this purpose or were to be used for this purpose, computations indicate that the radiation cost for the necessary amount of isotope would be about $2 or $3 per person instead of $200 per person.

Senator BRICKER. Where are they made now?

Dr. SWEET. At the Massachusetts Institute of Technology.

Senator BRICKER. Where do these commercial firms get the isotopes?

Dr. SWEET. They operate their own comparatively small cyclotrons.

Senator BRICKER. It is a high-cost operation?

Dr. SWEET. Yes, sir.

Senator BRICKER. What particular isotopes do you use?

Dr. SWEET. The one with which we have had our greatest experience by far is an isotope of arsenic, arsenic 74.

Senator PASTORE. You say if we could use the cyclotron at Oak Ridge, is there any question about it?

Dr. SWEET. The policy I believe at the moment has been, and perhaps Dr. Dunham or others will correct me on this, that the manufacture of cyclotron-produced isotopes has been turned over to commercial firms. It just happens that there is no commercial firm that has a massive cyclotron that operates at a high current, the type that is needed to produce efficiently this particular isotope.

Senator PASTORE. That doesn't sound to me to be a realistic answer, not that I am being critical of you. But just because they follow a policy of turning this over to private firms, and we recognize the fact that whereas it is now costing us $200 and can be made for $2 or $3, it is such an important thing that I can't see that is a valid reason for doing it.

Dr. SWEET. I am delighted to hear that you feel that way about it, sir.

Senator PASTORE. The chairman of this subcommittee will take that into account and get an answer.

Representative PRICE. We will certainly look into it. Is a cyclotron like a reactor? You can put in different material. You don't have to put in the same material every day. You can change.

(NOTE.—Representative Price requested the AEC for a statement on its plans for the production of arsenic 74. Mr. Price's letter and the AEC reply will be found in the appendix on p. 367.)

Dr. SWEET. Yes, sir.

Representative PRICE. You say they do not have any time at all at Oak Ridge to give to the production of this particular isotope. Can you comment on that, Dr. Albert?

Dr. ALBERT. I am afraid, Mr. Price, that I am not in a position to comment on the general reasons for the change in the policy, but by and large, I believe this particular isotope represents an unusual situation.

Representative PRICE. Will you try to get us the answer for that, because that seems to be a very interesting point, and appears to be something very worthwhile and important in the great work that Dr. Sweet is doing.

Dr. ALBERT. Yes, sir.

Dr. SWEET. We certainly would be very grateful if this isotope could be made available to others. We should like to have them check up on us.

Representative PRICE. You say it is available from commercial firms. Are there some commercial firms that do produce this particular isotope?

Dr. SWEET. There is one commercial firm that lists it in its catalog at $200 a millicure. It takes about a millicurie or a little more per person for this test.

Representative PRICE. Do they operate a cyclotron?

Dr. SWEET. Yes, sir. I am speaking of a firm in Pittsburgh that operates a comparatively small cyclotron.

Representative VAN ZANDT. Doctor, have you ever asked the Atomic Energy Commission to furnish the isotope from the Oak Ridge facility?

Dr. SWEET. We have been in correspondence about this, as a matter of fact, for a good many months. But I think that the members of the committee with whom we have spoken felt that this was a general policy regarding cyclotron-produced isotopes that they didn't feel they could override.

Representative VAN ZANDT. In other words, you do have an expression from the Atomic Energy Commission through this committee with whom you negotiated to the effect that this type of isotope is not available?

Dr. SWEET. That we should seek to make this available to our colleagues through commercial channels.

Senator BRICKER. How many commercial firms are producing the isotope?

Dr. SWEET. I know of only one that lists it in its catalog. Perhaps I am not fully informed on that score but I believe there is only one that lists arsenic 74.

Senator BRICKER. Are others preparing to enter the field?

Dr. SWEET. None that I know of. The firm, Abbott Laboratories, has, I think, been seeking to persuade the Oak Ridge group to use their cyclotron because Abbott has facilities right at Oak Ridge to take the irradiated target that has been bombarded in the cyclotron and prepare it for shipment in the appropriate form to the medical installations that would use it. My understanding is that Abbott Laboratories would be pleased to do the rest of the commercial preparation if the Oak Ridge cyclotron would just bombard the target.

Representative PRICE. Doctor, this committee will certainly pursue this matter further with the Commission.

Dr. SWEET. Thank you.

Representative PRICE. You regard it as an important factor in your work?

Dr. SWEET. I would be immensely pleased if others in the field could have this isotope available for their use. We have been accused in a friendly way of holding a monopoly on it.

Senator PASTORE. Did I understand you correctly, the way you tied this up, Dr. Sweet, is this: The only reason you are the sole users of this apparatus that Mr. Price remarked about is that others can't get these isotopes. If others could get the isotopes at a cheaper price, and they were available to more people, there would be more of these machines in operation?

Dr. SWEET. Yes, sir.

Senator PASTORE. Am I developing that correctly?

Dr. SWEET. Yes, sir. There are at least half a dozen people who have said that they would place an order for one of these machines immediately if they could only get the isotope.

Senator BRICKER. This is a diagnostic machine.

Dr. SWEET. Yes, sir.

Representative VAN ZANDT. How long has this isotope arsenic 74 been in existence?

Dr. SWEET. Its so-called decay scheme, all that goes on when this particular isotope breaks down, has been worked out for only about

5 years. In fact, our interest in its possible biological uses furnished a bit of a stimulus to some of the physicists at Massachusetts Institute of Technology to clarify finally its decay scheme and just exactly what happens when it disintegrates.

Representative VAN ZANDT. Was the initial isotope furnished by MIT?

Dr. SWEET. That is right with respect to the isotope used in patients. They continue to suppy us each week. In 3½ years we have studied about 700 patients now, all supplied by MIT.

Representative VAN ZANDT. So over a period of 3½ years this isotope has been in existence and has been made available to you through MIT?

Dr. SWEET. That is right, sir.

Representative VAN ZANDT. The AEC has had knowledge of this isotope and your anxiety is to acquire it at a much more reasonable price?

Dr. SWEET. I should say that we have not paid $200 a millicurie for it. Through the kindness of the MIT physicists, we have had it at a very much lower figure.

Senator PASTORE. Doctor, have you any figures on how many people die of brain tumor in the course of a year?

Dr. SWEET. A substantial number die from tumors that jump to the brain from other organs in the body, especially if they jump in multiple fashion to the brain, so that there are a good many of them scattered through the cerebral hemispheres. I am sorry to say that we have no surgical tactic that is of any use in managing those patients.

Of the patients that might conceivably be candidates for efforts to treat their tumors, approximately somewhere between 2 and 20 per thousand hospital admissions have a brain tumor in a large general hospital. This represents a comparatively small number.

Senator PASTORE. Have you any figures as to the number of people that involves?

Dr. SWEET. I am sorry I cannot cite those.

Senator PASTORE. Can you give us an approximation? There are thousands and thousands of people that die from brain tumors. I am afraid when you speak of 0.2 and 2 percent, it does not ring any score with the people.

Dr. SWEET. Unfortunately from the standpoint of giving you statistics for the 160 million people in this country, I just can't do that.

Senator PASTORE. That is difficult.

Dr. SWEET. Those would certainly be available.

Senator PASTORE. I wonder, Mr. Chairman, if a member of the staff could get that figure?

Representative PRICE. I think it would be advisable to do that. I imagine there are some accurate figures on it. I think it should be included at this point in the record. The committee staff will seek those figures.

(The information referred to follows:)

According to the death reports from the States of the Union published in the Annual Statistical Bulletin of the United States Bureau of Vital Statistics by the Government Printing Office in Washington, D. C., there were in the United States 7,246 deaths from tumors of the brain and spinal cord in 1952 and 7,570 such deaths in 1953. (The overwhelming majority are brain tumors). In

addition thre is a similar but lesser number of patients who have had such tumors successfully removed, so that they die from other causes. On the basis of these data we estimate about 14,000 people or less per year in this country have brain tumors.

Dr. SWEET. I might show you a few more of these scans. This (exhibit 95) happens to be one on a patient who was thought to have no chance of having a brain tumor, because she had recovered completely from a serious episode of illness involving the brain. Only 2 years later did her condition again begin to deteriorate. It was thought that she had another entirely different type of disease called multiple sclerosis. Actually this scan demonstrated a marked concentration of this isotope behind the ear and the next scan (exhibt 96) shows the right-sided location of the tumor. On the basis of these scans we were able to diagnose and remove this tumor, whereas her clinical history had been so deceptive and so lacking in a suggestion of tumor that she would not have been submitted to a surgical diagnostic measure with tumor in mind. Only by virtue of the fact that we had this harmless and painless measure open to us did we make a correct diagnosis.

EXHIBIT 95. Tumor (meningioma) in right posterior cranial fossa—coincidence scan—positrocephalogram.

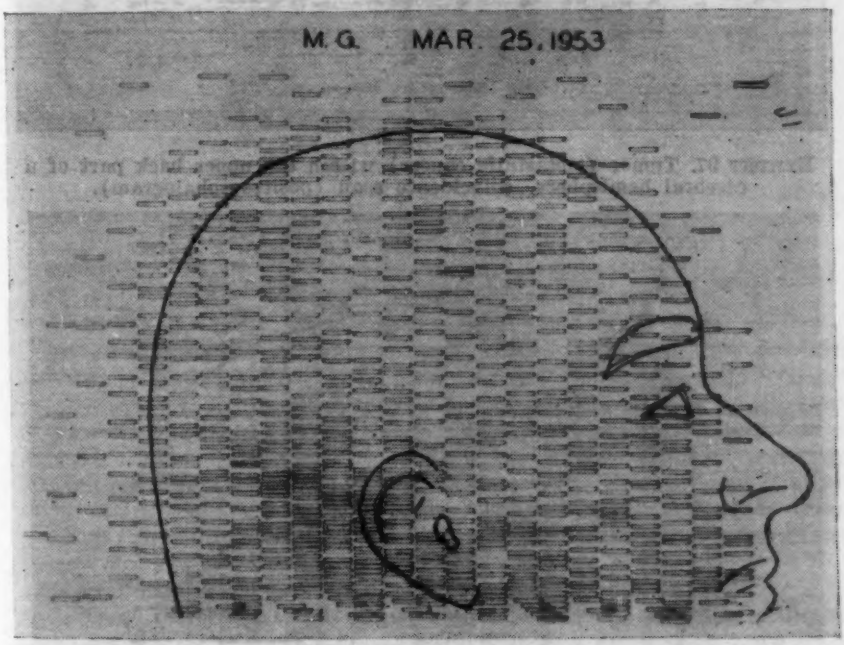


EXHIBIT 96. Tumor (meningioma) in right posterior cranial fossa—scan of asymmetry—asymmetrogammagram.

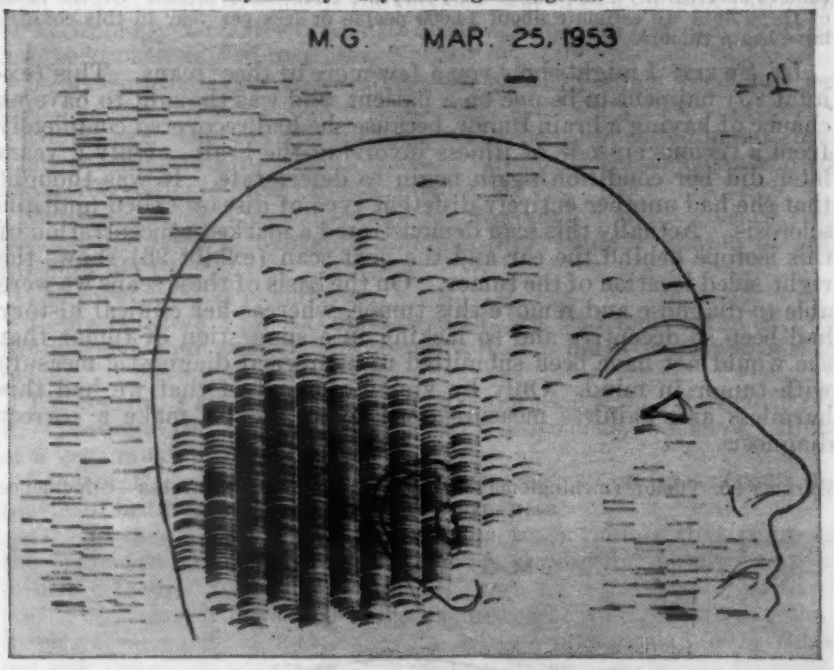
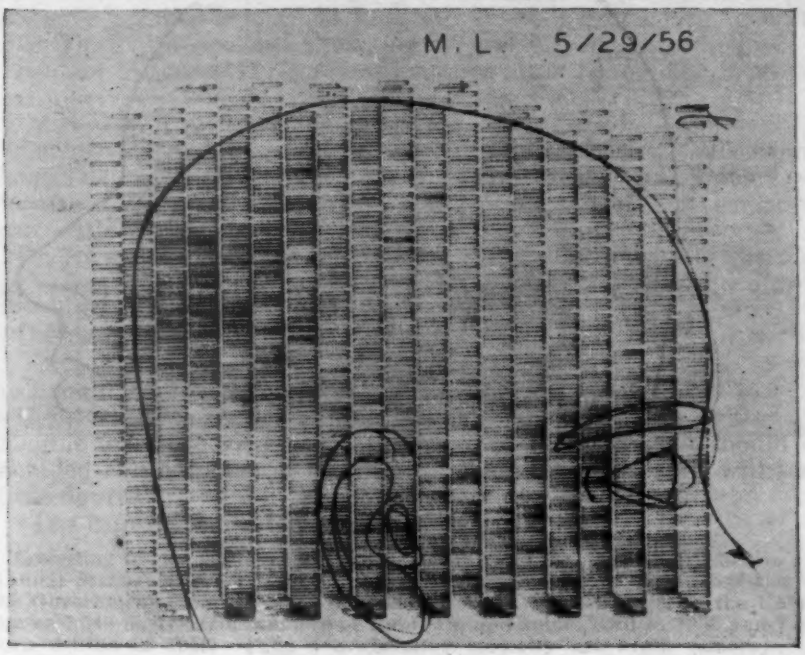
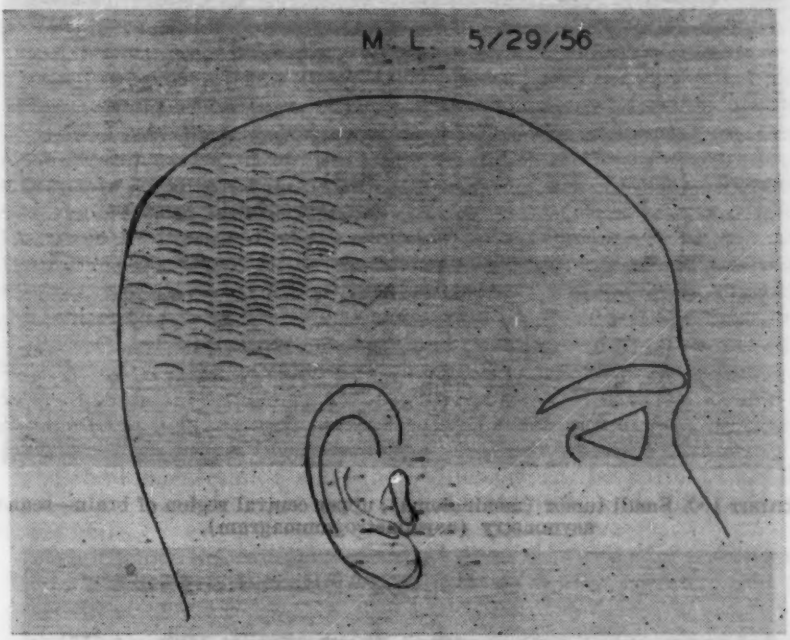


EXHIBIT 97. Tumor (metastatic cancer) within the upper back part of a cerebral hemisphere—coincidence scan (positrocephalogram).



The next figures illustrate the way in which we can at times get a less striking indication of tumor in some of these scans. In exhibit 97 one can make out the area of increased density in the back of the cranial area. The next figure (exhibit 98), which is of the same patient, shows that the marks of asymmetry are not nearly as dense as in exhibit 96, and this tumor lay deep within the substance of the brain. It too was totally removed with a favorable early result.

EXHIBIT 98. Tumor (metastatic cancer) within the upper back part of a cerebral hemisphere—scan of asymmetry (asymmetrogammagram).



The next figure depicts one of the small tumors. This patient had previously had both of the surgical diagnostic measures of X-ray photography after injection into an artery, and also after replacement of cerebrospinal fluid by air. Both of these came out to be entirely normal. Exhibits 99 and 100 show that the lady did have a tiny tumor on the surface of the left cerebral cortex. By removing it at an early stage, we were able to spare her cortex, and save her from paralysis that might follow our removal of a tumor 2 or 3 times that size.

I have more slides, but I think I have consumed my time.

Representative PRICE. I hope you will not limit your time if you have something of importance to tell. It is a subject that we have been greatly interested in. I hope you will not feel you are taking too much time of the committee. We want to hear a report on your work.

For instance, we would like to know more about how you are succeeding in the treatments at the Brookhaven Laboratory. Could you give us a résumé of the number of treatments you have had and some of the results of the treatments, and what progress has been made there in the last year? It has been almost 2 years since this committee

EXHIBIT 99. Small tumor (meningioma), upper central region of brain—coincidence scan (positrocephalogram).

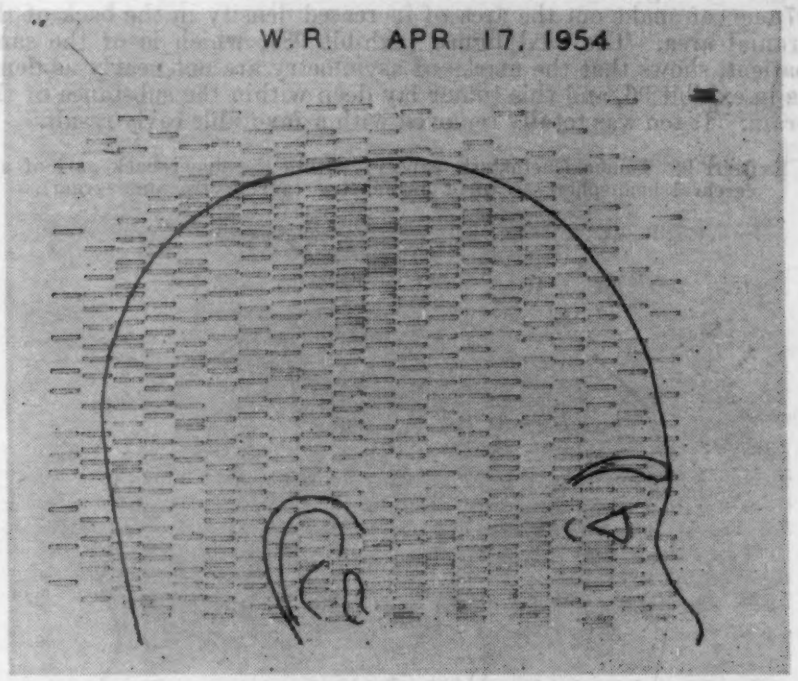
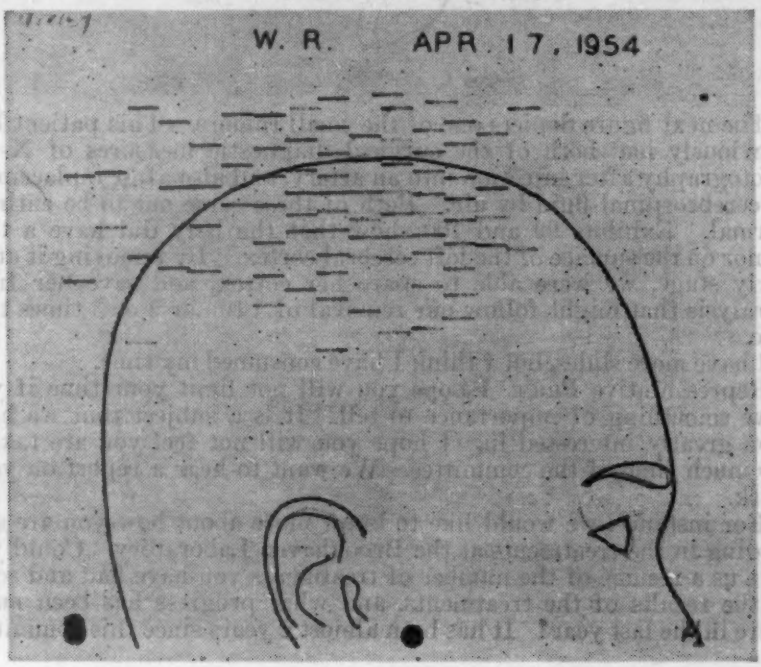


EXHIBIT 100. Small tumor (meningioma), upper central region of brain—scan of asymmetry (asymmetrogammagram).



ran a check on this program. I am wondering what progress you made in that 2 years' time. Could you give us a résumé of that program?

Dr. SWEET. We have encountered one major difficulty in our management of these patients to date, namely, that the scalp has taken up a good deal of this boron-containing compound which we have used in the treatment. When the boron in the skin has captured some of the slow neutrons emerging from the reactor, the destructive reaction which we want to occur in the brain also occurs in the skin.

Representative PRICE. For the purpose of the record, will you tell us the nature of the treatment, and then expound on your difficulty?

Dr. SWEET. Very good, sir. Utilizing again this same phenomenon of rejection by the normal brain of substances circulating in the bloodstream, we inject into the bloodstream compounds of the element boron. There is one isotope of boron that has a peculiar and tremendous affinity for these tiny particles called slow neutrons that can be made to emerge from a nuclear reactor. When this appropriate isotope of boron, boron 10, captures a slow neutron, it immediately disintegrates into two particles, each of substantial size. These travel almost no distance at all in tissue; they give up all of the enormous energy typical of an atomic disintegration within a few thousandths of a millimeter. So that this means that the destructive energy will be confined virtually to the cell in which the boron atom happened to lie. Hence if a tumor cell would take up a good deal more boron 10 than a normal neighboring brain cell, the normal cell would survive and the tumor cell would die from this form of radiation. This is in effect an effort to get the tumor cells to commit suicide by taking up out of the bloodstream a substance which, when the patient's head is exposed in a nuclear reactor, will disintegrate and kill only the tumor cells.

Other tactics for radiation don't possess this peculiar differential effect. They will tend to kill normal cells as well as the cells that one wishes to kill.

In order to use this principle at the present time, we have been irradiating the patients with the skull and scalp intact after an operation to remove most of the tumor. We are left post operatively with a patient in whom there is a brain that looks to the surgeon to be normal, and yet it contains tumor infiltrating it like the roots of a tree growing into the ground. We can't take out these tumor remnants without sacrificing indispensible normal brain. So our effort has been to try to get these little rootlets of tumor killed with this technique of slow neutron capture by boron 10.

As I say, we have been carrying this out through the intact skull and scalp. When we do this, we have had such bad burns of the scalp, when we have elevated the neutron intensity to a high level, that this burn has constituted a major disadvantage of the method. We need to use an arrangement whereby this hole in the nuclear reactor, the so-called portal, will open into a room that is surgically sterile, like an operating room. Then we can elevate our bone flap again and expose the area of the brain so that our neutron beam can be directed right at the exposed face of brain which looks normal but contains tumor.

When we are able to do this, we shall, of course, avoid the extreme scalp burn which Dr. Farr and I have felt at the present time precludes our repeating the tactics we have used in the past.

As you know, a new medical reactor, so-called, is in the process of construction there. We have not felt warranted in submitting any patients at the facility now available to this form of treatment in which the brain is exposed directly to the neutron beam.

Senator PASTORE. Dr. Sweet, the last time I talked with Dr. Farr—it was only a casual conversation with reference to this matter of burning the outside of the head—he said he was trying to develop a theory of slowing down the neutron and then speeding it up once it got inside the skull. Has anything ever become of that?

Dr. SWEET. I wonder if you did not have this in mind. If the neutrons that emerge from the reactor have not already been slowed down to the so-called slow-neutron range—if, as they are going through the skull and the scalp, they are still in a range that is faster than that, then they won't be captured by the boron in the scalp, but they will rather quickly slow down in the tissue inside the head to the range where they can be captured. That is a point on which we have been working, to see if we can use a so-called epithermal beam.

Senator PASTORE. Is it fair to assume that where there is a tumor pretty well deep in the skull that the treatment that has been heretofore used has become more or less obsolete at Brookhaven in 2 years?

Dr. SWEET. We see this possibility of doing so much better, of avoiding this problem of the delayed late burns of the scalp——

Senator PASTORE. You mean by opening up the skull and exposing the diseased part to the direct neutron?

Dr. SWEET. Yes, sir.

Senator PASTORE. Have any experiments been conducted?

Dr. SWEET. Only on animals. With animals we are not concerned about a burn of the skin as we are in man. When we irradiate them, Dr. Farr has some clear-cut studies which show that the treatment is indeed effective in this situation.

Senator PASTORE. You mean by exposure?

Dr. SWEET. Yes; to the slow neutron beam that we now have.

Senator PASTORE. Where have you conducted those experiments?

Dr. SWEET. They have been done at the Brookhaven reactor under Dr. Farr's direction.

Representative PRICE. I believe Dr. Farr will testify later.

Dr. ALBERT. Yes; he will present a paper on this subject tomorrow.

Representative VAN ZANDT. Doctor, the last time we were at Brookhaven they had a young doctor from upstate New York who received the treatment. I can't recall his name. I wonder if you do, and if so is he still alive?

Dr. SWEET. A young doctor? I don't remember that patient. That may be somebody that Dr. Farr was treating that I don't know about.

Representative PRICE. Are there any patients who received the treatment at Brookhaven still alive?

Dr. SWEET. I am sorry to say that none of those patients with whom I have been directly connected are now still alive.

Representative PRICE. I think for the purpose of the record you should show the type of patients that you gave the treatment to at Brookhaven.

Dr. SWEET. Yes, sir. I think we ought to emphasize that they were people not only known to have a hopeless kind of tumor, but to have it in an advanced stage. We felt in the early phases of studies of this

sort that such were the patients on whom we should seek to find out the disadvantages as well as the possible advantages of the method.

Representative PRICE. Do you feel that in any of the cases where treatment was recived that any benefit came to the patients?

Dr. SWEET. We had some clear-cut evidence of so-called remission. That is to say, an individual who was showing serious neurological signs had improvement of those signs. Unfortunately, this betterment was not permanently maintained.

Representative PRICE. Do you feel that there was any incidence of prolongation of life through the treatment?

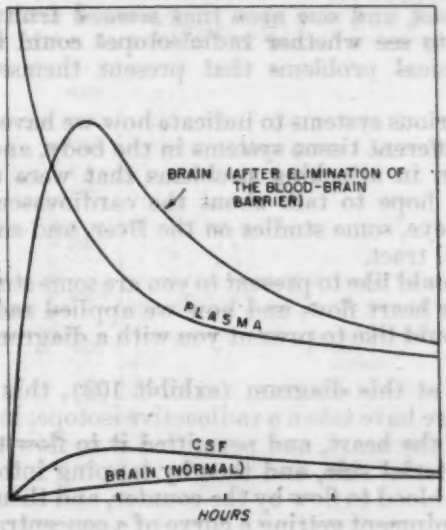
Dr. SWEET. We had two series of patients at Brookhaven; in the first series a much smaller dose of radiation was given to each patient than in the second series. In the second group the average length of life was greater than in the first series. I am really cribbing Dr. Farr's material.

Representative PRICE. Dr. Farr will testify tomorrow. Of course, we also knew of your great interest in that work and the fact that you participated in many of those experiments and many of the patients were your own patients.

Will you proceed with whatever you wish?

Dr. SWEET. May I show the last slide. This (exhibit 101) summarizes the behavior of radiophosphate in normal and abnormal areas of the brain. My colleague, Dr. Louis Bakay, who managed to escape from Hungary 9 years ago, has been working with us for the past 8 years. He has carried out some careful studies to show that when any sort of injury occurs to the brain there is a breakdown of the barrier between it and the blood. Then instead of taking up the small amount of isotope indicated on the line at the bottom of the graph, the injured brain takes up an enormous amount of isotope as shown in the top line.

EXHIBIT 101. Studies of Dr. Louis Bakay. Uptake of Radiophosphate from blood by normal brain, injured brain, and cerebrospinal fluid.



We are proposing, for example, to use this tactic to see if we can find areas of abnormal or pulpified brain in patients with acute head injury in whom it may be exceedingly difficult by any clinical means to demonstrate that there is a focal area of damage to the brain. The surgeon might remove such a swollen destroyed area as an emergency measure and save such a patient with acute head injury from death.

Another possible application of this tactic is in the locating of the site of a hemorrhage inside the brain such as may occur in an apoplectic stroke. In the past our tendency has been to operate on only a few of these patients, because we have not been able to spot the hemorrhage or even be sure there was one in many instances. Yet, as we studied this group, we realized that the surgeon ought to be able to evacuate a good many of these life endangering hemorrhages and save the patient. We hope this tactic will assist us in spotting the exact site of such a hemorrhage, so that we can remove it while there is still time to prevent the patient from dying.

Thank you.

Representative PRICE. Thank you very much, Dr. Sweet. You have given us a very interesting and informative presentation.

Dr. ALBERT. The next medical scientist to testify is Dr. Hymer Louis Friedell, who is the director of the department of radiology, Western Reserve University School of Medicine, and was also director of the atomic energy project at this school also. He will discuss some diagnostic uses of radioisotopes in medicine.

Representative PRICE. Dr. Friedell, the committee will be pleased to hear from you.

STATEMENT OF DR. HYMER LOUIS FRIEDELL, DIRECTOR, DEPARTMENT OF RADIOLOGY, WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE, CLEVELAND, OHIO

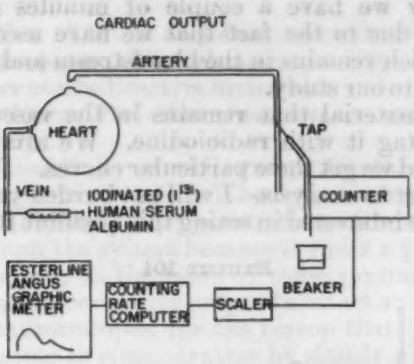
Dr. FRIEDELL. Mr. Chairman, and ladies and gentlemen, as a professor of radiology, I have been interested in the use of radiation for various purposes, and one area that seemed fruitful to study, and examine, was to see whether radioisotopes could be applied to the diagnostic clinical problems that present themselves in everyday medicine.

I selected various systems to indicate how we have approached these problems in different tissue systems in the body, and what usefulness they have been in attacking problems that were difficult to attack previously. I hope to talk about the cardiovascular system, some studies on the eye, some studies on the liver, and some studies on the gastrointestinal tract.

The first I would like to present to you are some studies on measuring cardiac flow or heart flow, and how we applied radioisotopes to this problem. I would like to present you with a diagram which I think is explanatory.

If you look at this diagram (exhibit 102), this is schematic and indicates that we have taken a radioactive isotope, introduced it on the venous side of the heart, and permitted it to flow through the heart and out the arterial side, and then by tapping into the bloodstream, permitting the blood to flow by the counter, and then by use of a series of detecting equipment getting a curve of a concentration of the radioactive material in the blood.

EXHIBIT 102



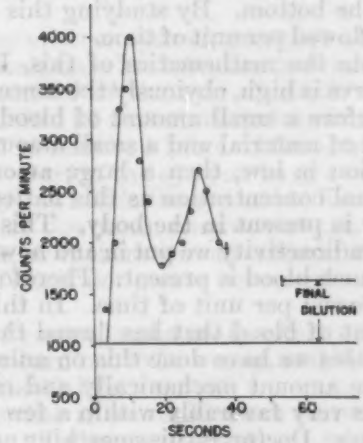
It has been known for a long time, particularly by hydraulic engineers, that if you want to know something about the flow of any system, if you can introduce some material, the concentration of which can be measured, then by the way in which the concentration is altered you have lots of information about the flow. You can even quantitate this and tell quantitatively how much flow has occurred in any unit of time.

This is the main objective that we had in this particular study. If you will look in the lower corner you will see a curve that was drawn by this equipment.

Representative PRICE. Without objection all these charts will be included in the record.

Dr. FRIEDELL. This is the character of the curve (exhibit 103) and you can see that it has a very large hump, which is due to the fact that the material has been first introduced and has not been diluted completely. Then you see a smaller hump which means that the material has come around again.

EXHIBIT 103

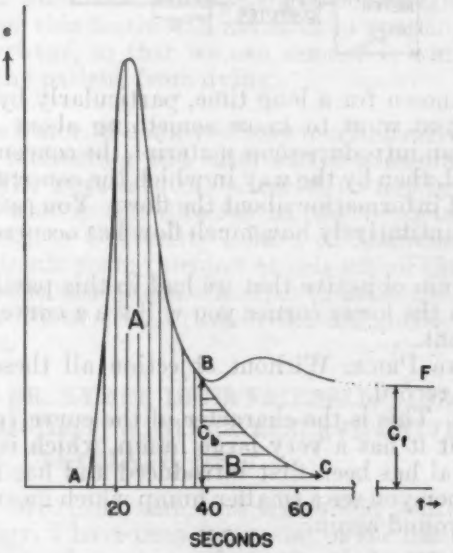


Finally then it flattens out after a long period of time, a few minutes—actually we have a couple of minutes shown here—and this flattening is due to the fact that we have used a special radioactive isotope which remains in the bloodstream and does not leak out. This is important to our study.

So we take a material that remains in the vascular system, such as albumin, and tag it with radioiodine. We are then prepared to make the study and we get these particular curves.

These are subject to analysis. I will not burden you with the analysis, but you may be interested in seeing this (exhibit 104).

EXHIBIT 104



The analysis can be simply made by studying the first curve and extrapolating it to the bottom. By studying this curve, we can then tell how much blood flowed per unit of time.

Without going into the mathematics of this, I can tell you very simply that if the curve is high, obviously the concentration must have been high, and therefore a small amount of blood must have flowed, because there is a lot of material and a small amount of blood.

If the concentration is low, then a large amount of blood must have flowed. The final concentration as this flattens out tells us how much blood actually is present in the body. This is done simply by knowing how much radioactivity we put in and how much it is diluted; we then know how much blood is present. Therefore, we can tell how much of the blood flowed per unit of time. In this way we actually quantitate the amount of blood that has flowed through the heart.

In order to check this we have done this on animals whereby actually we measured the amount mechanically and compared it to this method, and it checks very favorably within a few percent.

Representative PRICE. Doctor, is this something new?

Dr. FRIEDELL. Yes; this is a new approach.

Representative PRICE. It was developed strictly through the use of radioisotopes.

Dr. FRIEDELL. Yes. This is a system which has been devised primarily with radioisotopes, although attempts have been made previously by using other nonradioactive materials.

Representative PRICE. Did that function as well with the nonradioactive materials?

Dr. FRIEDELL. Essentially as well, except for this one very important point that I wish to come to. When you use radioactive isotopes you are now able to measure the concentration without actually getting the material out from the system because it emits a particle which you can detect. Therefore, on the basis of these preliminary studies, we have been able to measure cardiac output in intact animals. This is not possible without radioisotopes, for the reason that you can detect the isotope and its changes in concentration by simply placing the counter in a strategic position and drawing these curves.

So on the basis of these original studies, we are now able to make estimates of the cardiac flow in intact animals because we are able to use a radioisotope which emits radiation that can be detected outside the body.

Senator PASTORE. Doctor, for the purposes of the record, will you tell us where that will lead? What will we prove?

Dr. FRIEDELL. This is one of the very important measures in determining cardiac function. Since we are now able to attack various heart problems by surgery and other ways, this is an important parameter in making a decision whether the function has been modified satisfactorily or not. So a simple method which this may prove to be could in a very important way help in determining cardiac function.

Representative PRICE. In other words, the true value of this is in diagnostics.

Dr. FRIEDELL. Yes, that is correct. There are some other corollaries of this but I will not burden you with them. I think the main point is that it is possible with such a system to make measurements that are accurate and give you some studies that we could not have made previously.

Now, to change to another system, one of the things we have been interested in for a long time has been the determination of the degree of malignancy of tumors of the eye. I think everyone who is familiar with the problem of tumors understands that the best way to diagnose a tumor is to remove a piece of tissue and examine it under a microscope. However, in the eye you have a very special problem, because the tumor grows inside the eye and to have access to the tumor generally means that you must remove the eye. If the tumor was not a malignant one, or if there was an error in diagnosis, the patient has lost his eye. This is not a rare occurrence in hospitals over the country.

The clinicians, of course, make every effort to be right, but every once in a while they turn out to be wrong, and they accept this risk in order to save the patient's life.

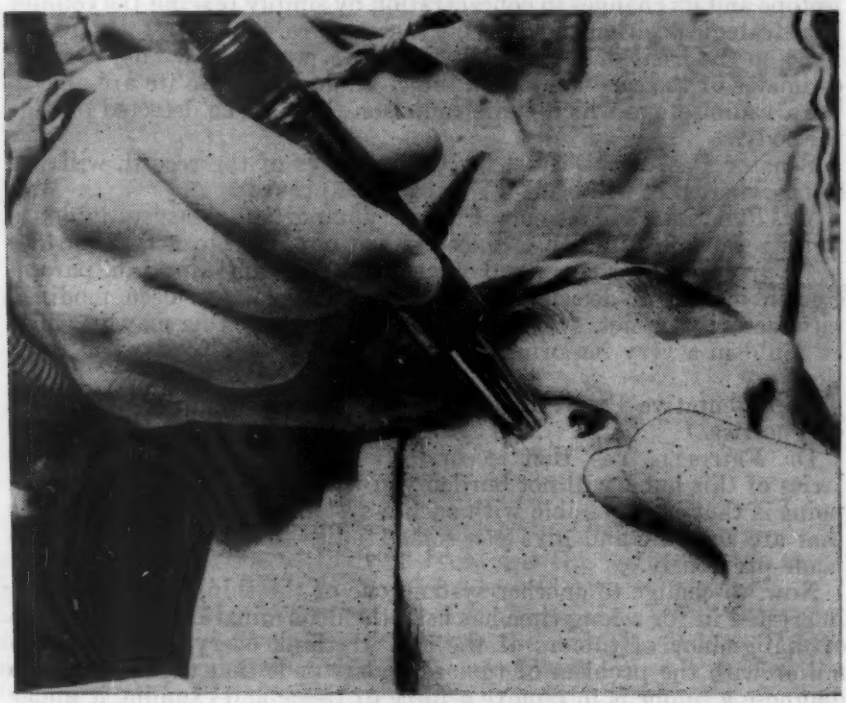
It occurred to us that if we could use a suitable isotope, we could attack this problem. Tumors will selectively take up certain isotopes, and one of these that is very useful is radiophosphorous. If you intro-

duce radiophosphorous into the body in the form of sodium hydrogen phosphate, there will be some selective uptake in malignant tumors. This has been known for a long time.

The beta particle emitted by the phosphorous is energetic enough to escape from the eye. If we have the right kind of measuring device, we can then compare the suspected site to a normal site, and see whether there has been any increase in the uptake. This is essentially what we have done.

This is a photograph again which shows how this is done (exhibit 105). This is done very simply by using a Geiger counter which is applied over the site, and then the counts are made in this area. This is compared to a normal site, and the differential ratio is then determined.

EXHIBIT 105



We have now done over 80 cases, and here is a study of the first few cases which shows in this chart (exhibit 106) these black areas which represent the increase above the expected ratio. If a tumor is not present, obviously the ratio ought to be 1 to 1. If a tumor is present, the ratio increases beyond one.

EXHIBIT 106

TEST RESULTS FOR CASES WITH PROVEN* DIAGNOSES

Case No.	Date	Ratio of Tumor to Normal c/min In Vivo		In Vitro	Disposition & Remarks	Pathological Findings (P) or Clinical Diagnosis (C)
			ANTERIOR TUMORS			
3	2-51		2.30	5.62	Enucleation for tumor	Melanoma of Choroid (P)
7	7-51		2.26	3.49	Enucleation for tumor	Melanoma of Choroid (P)
22	6-52		1.94	6.85	Enucleation for tumor	Melanosarcoma Choroid (P)
38	3-53		1.79	1.91	Enucleation for tumor	Melanoma of Choroid (P)
27	7-52		1.74	6.23	Enucleation for tumor	Melanoma of Choroid (P)
4	3-51		1.66	4.68	Enucleation for tumor	Melanosarcoma Choroid (P)
5	3-51		1.65	4.89	Enucleation for tumor	Melanosarcoma Choroid (P)
2	1-51		1.50	No Spec.	Enucleation for tumor	Melanoblastoma Choroid (P)
33	11-52		1.47	-	No procedure	Metastatic Ca (Breast)(C)
9	9-51		1.42	-	No procedure	Metastatic Ca (Breast)(C)
35	1-53		1.41	1.90	Enucleation for tumor	Melanoma of Choroid (P)
			POSTERIOR TUMOR			
14	2-52		1.27	14.23	Enucleation for tumor	Melanoma of Choroid (P)
18	5-52		1.24	No Spec.	Enucleation for tumor	Spindle-cell Ca (P)
17	5-52		1.21	3.82	Enucleation for tumor	Melanosarcoma Choroid (P)
			RETINOBLASTOMA			
37	2-53		0.95	5.40	Enucleation for tumor	Retinoblastoma (P)
43	4-53		1.15	-	X-Ray therapy	Retinoblastoma in second eye, first eye enucleated (P)
			NON-TUMORS			
15	4-52		1.31	-	Enucleated for Uveitis	Uveitis (P)
34	12-52		1.23	-	No procedure	Uveitis (C)
26	7-52		1.20	-	Operated for hemorrhage	Proven hemorrhage (P)
6	5-51		1.20	-	Reattached	Fluid detachment (C)
40	4-53		1.18	-	No procedure	Uveitis (C)
24	7-52		1.15	-	Enucleation for tumor	No tumor (P)
11	11-51		1.13	-	Reattached	Fluid detachment (C)
13	1-52		1.09	-	No procedure	Uveitis (C)
31	9-52		1.08	-	Reattached	Fluid detachment (C)
32	10-52		1.06	-	Reattached	Fluid detachment (C)
19	6-52		1.05	-	No procedure	Uveitis (C)
25	7-52		1.05	-	Reattached	Fluid detachment (C)
10	10-51		1.03	-	No procedure	Old healed inflam. lea (C)
41	4-53		1.02	-	No procedure	Benign Melanoma of Iris (C)
8	9-51		1.02	-	Enucl.-sec. glaucoma	Uveitis (chronic) (P)
20	6-52		1.02	-	Reattached	Fluid detachment (C)
1	12-50		0.98	1.00	Enucleation for tumor	Fluid detachment (P)
30	9-52		0.95		Retina completely det.	Fluid detachment (C)

Measured, but not included in this table are: 1 probable anterior tumor, refused enucleation, 8 cases with inconclusive results, to be observed and subjected to further measurements.

*By "proven" diagnoses is meant: 1. Definite pathological findings. 2. Successful reattachment. 3. Classical clinical findings.

In these instances we have had ratios going up as high as 5 and 6, and in every instance wherever the ratio was above 1.5 this definitely turned out to be a tumor. This has been very effective in helping us to differentiate various tumors of the eye, and has, I am sure, saved several eyes in our own institution.

So we have used this method for studying all eyes that may be subjected for surgery for this reason.

Senator PASTORE. How prevalent is this in other institutions?

Dr. FRIEDELL. There have been reports by others who have had reasonably good success. I am sorry to say they don't seem to have the same success we have had apparently because we have been more interested. Others have used it and do use it in special problems. I would guess, and this is purely a guess, that perhaps 30 to 50 insti-

tutions are using this approach to determine whether or not a tumor is present in the eye.

Senator PASTORE. What was the diagnostic treatment before this use of radioisotopes?

Mr. FRIEDELL. Ophthalmologists who are familiar with eye tumors and other lesions of the eye would examine the eye carefully and do other studies that were purely clinical but could never have the tissue to examine under the microscope which is really essential in determining the tumor. They would base their diagnosis on their clinical ophthalmoscopic observations and the clinical examination of the patient. This was the only method they had previously for determining whether or not a malignant tumor was truly present.

Senator PASTORE. Which by no stretch of the imagination could be positive diagnosis.

Dr. FRIEDELL. They could not really be certain until the eye was removed and examined.

Senator PASTORE. What would be the result of that? Would it be blindness in that eye?

Dr. FRIEDELL. With removal of the eye, of course, the eye is gone. This is generally an unhappy circumstance if the eye could have been saved for any reasons.

Representative VAN ZANDT. Doctor, what figure did you use a moment ago in regard to the number of patients you had?

Dr. FRIEDELL. We have done approximately 80 patients.

Representative VAN ZANDT. Of the 80, in how many did you actually find a tumor?

Dr. FRIEDELL. We have been able to show a positive identification of tumors in all but one. In other words, 79 of the 80.

Representative VAN ZANDT. Did all of them submit to an exploratory operation?

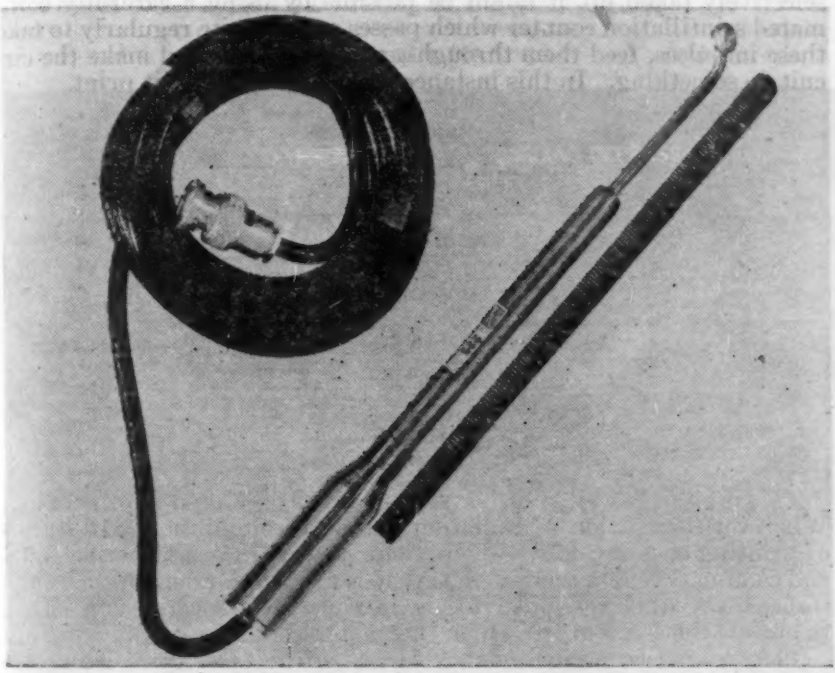
Dr. FRIEDELL. Yes; in those instances.

There has been even during this study at least one eye removed that did not have tumor—because the study was early. The ophthalmogists were not certain that our studies were really specific. They felt so certain clinically that this was a tumor that they removed it. Our studies had previously shown that the differential uptake was not high enough to warrant the diagnosis from our point of view. These turned out to be not tumorous. It gave us further reason to believe that this is a good approach.

One of the important problems in this, and one reason why it may not have met with as much success as it should on the outside is that many of these tumors occur posteriorly. It is necessary to apply the counter directly over the tumor site. The proper kinds of instruments were not always available. Very recently we have developed a special

counter which is curved and may be inserted behind the eye to approach these sites and should help even further in making these diagnoses. This is what it looks like. (Exhibit 107.)

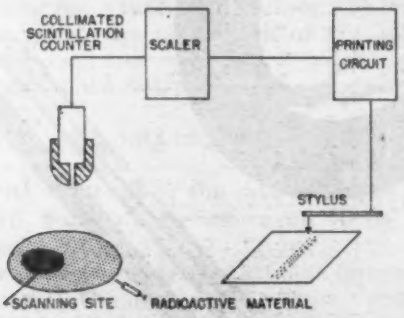
EXHIBIT 107



One very important study that we wanted to do and have been thinking about for a long time has been the use of radioisotopes which might be selectively deposited in various organ structures. If these radioisotopes were so deposited, it might be possible to use the radiation coming from these radioisotopes to outline the structure itself. This is somewhat similar to the use of ordinary X-rays. In ordinary X-rays you have a source of X-rays which come through the body, and then are recorded on a photographic film. The reason why you are able to visualize this—nobody really sees X-rays; they see the effect on the film—is that here is a differential absorption of X-rays as they traverse the body. The denser substances and the denser structures absorb the X-rays and therefore you see this differential when you look. If we could get differential uptake of radioisotopes—that is, by putting it into the body or into the vascular system and letting the deposit preferentially some place—it might be possible to use the radiation coming from this organ system to take a look at the structure itself. We therefore made an attempt to see if we could do this with a tissue system which appeared to offer the greatest promise—that was the liver.

The system as we use it essentially is of this character, and I might briefly go into the diagram here (exhibit 108). This lower site is called the scanning area of the radioactive material and is really supposed to represent a cross section of the body. If you introduce radioactive material and use the proper kind of radioactive element so that it is selectively taken up, it might be possible by using a carefully collimated scintillation counter which passes over the site regularly to take these impulses, feed them through a proper circuit, and make the circuit do something. In this instance what we do is have it print.

EXHIBIT 108



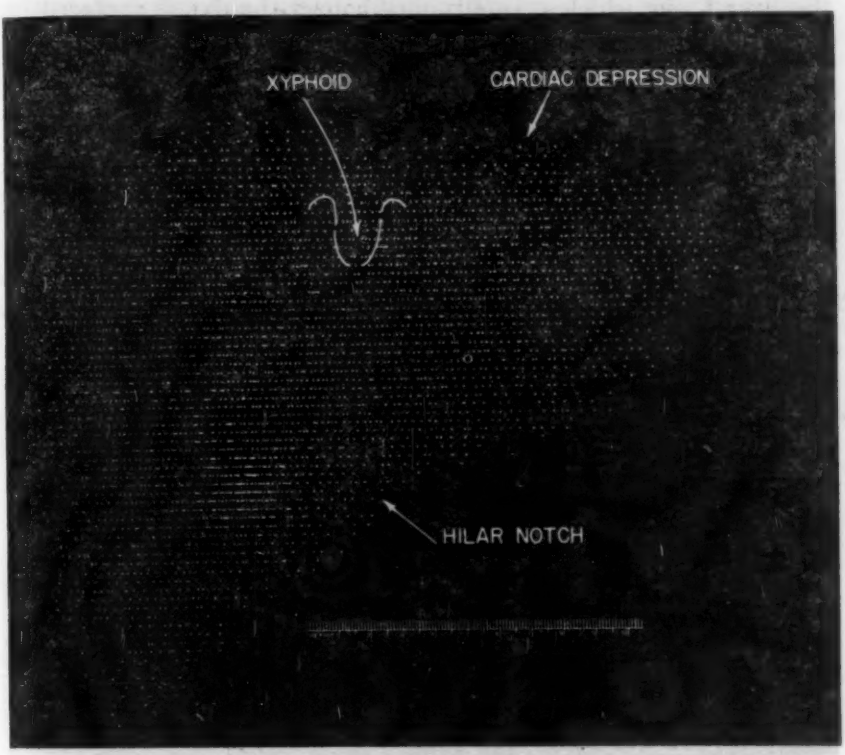
This is a fairly well known system that has been used in other ways. Wherever there is lots of radiation coming through, there will be lots of printing or many dots. Where there is very little radioactive material coming through, there will be very few dots. Under these circumstances, it would be possible, if there is really good selective deposition, to outline the structure in which this material is deposited.

The system that we looked at as I have said was the liver. There are many substances which are readily metabolized by the liver. That is, the liver handles them for various reasons, and they are selectively taken up by the liver if you introduce them into the blood. We looked into a number of these. The two most important were Rose Bengal and tetraiodophenolphthalein. The tag in these instances is iodine 131, which has a nice energetic gamma ray that we can detect outside the body. We find that these materials will be metabolized primarily by the liver. So we then began to do our study.

One of the important things we found was that it was necessary to introduce a special circuit which would trim out extraneous radiation. So if the differential radioisotope uptake was comparatively modest, we could improve or intensify this result by throwing away the low-level radiation—leaving us with a higher concentration and a sharper image. We began to do our studies and were able to begin to show some pictures of the liver.

This is a perfectly normal liver (exhibit 109). It looks like the map of Africa on its side, and is fairly distinctive of the liver, and has the appearance, as you see it often by X-ray alone. You can see a little area of density in the lower margin. This is the gall bladder. Some of the dye is actually excreted rapidly, and enters the gall bladder, and you begin to see some visualization of the gall bladder.

EXHIBIT 109



You might argue that this gives a fairly good gross description, but there is no fine detail. This is essentially true. Very fine detail might escape us, but the modifications in the liver are often great enough so that we can depict them by making this kind of study.

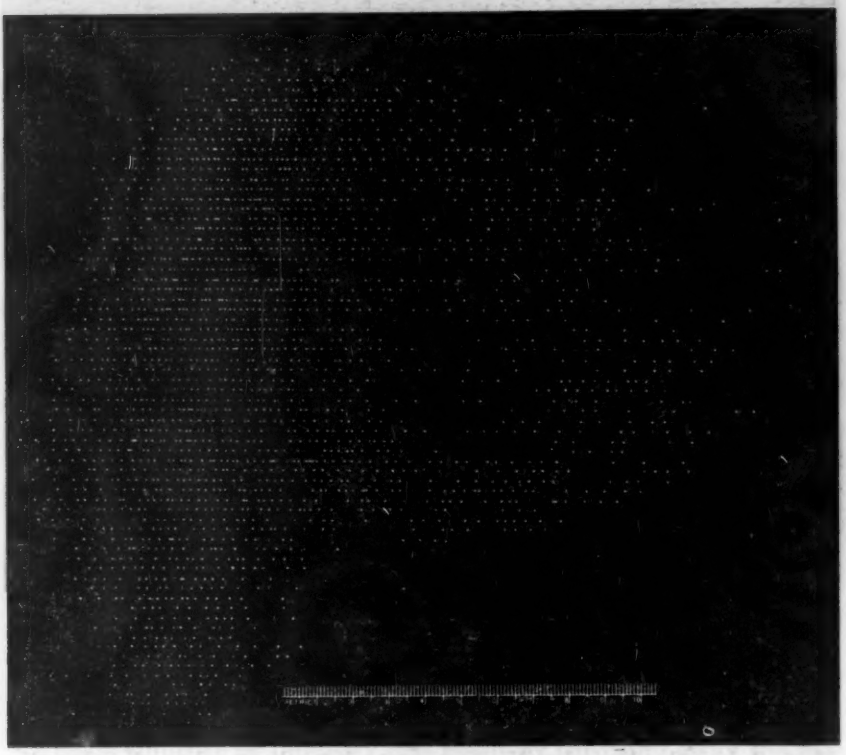
This is important because the only methods we have had previously of studying the liver by X-ray was to introduce a long-lived radio opaque radioactive material that lasted in essence forever and was quite dangerous for this reason, and has long since been discarded.

Another method that has been used was possibly to operate on the patient, put a dye into the blood as it enters the liver, and this in

essence would opacify the liver. X-ray examination might perhaps show some modifications. None of these methods are readily applicable. This, if it proves to be useful, should give us a great deal of information about the structure of the liver. Here are some of the first studies that we did, and you can compare them with the original.

This patient had a cancer of the liver (exhibit 110), and you can see the defects that are present in this liver structure. Obviously there are areas there that do not take up the dye. The reason for that is that the liver tissue which normally metabolizes the dye is replaced by tumor tissue which has no function in this respect, and therefore does not take it up. When the machine scans this, it recognizes that no radioactivity is present, and makes this record.

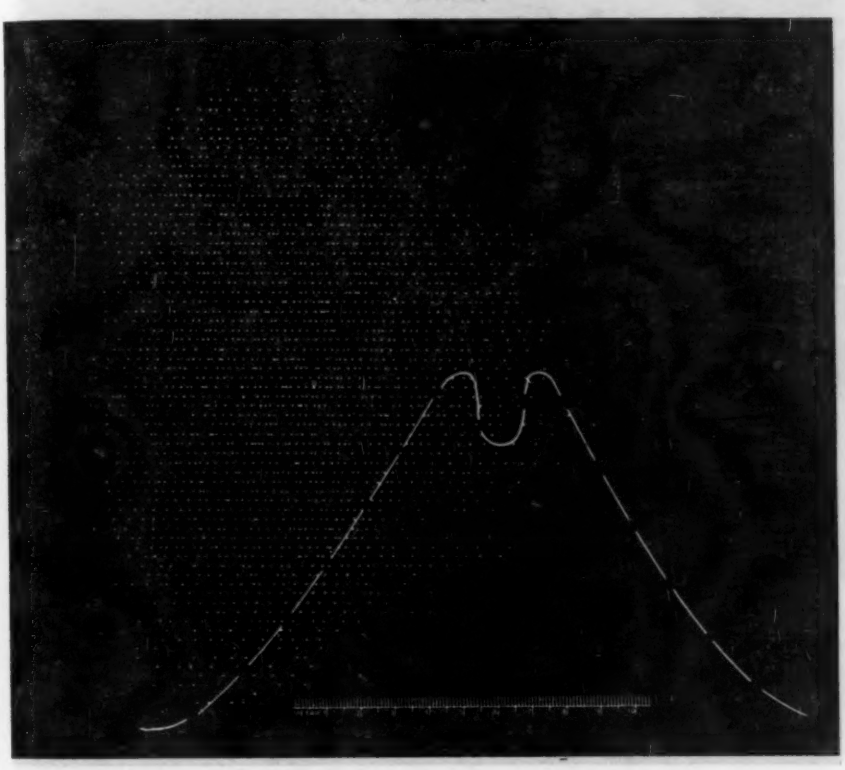
EXHIBIT 110



We have a great deal of these that show very clearly that we may demonstrate defects in the liver when we use this system.

Here is another good example (exhibit 111). This is a patient who previously had the left lobe—in other words, the left half of his liver—resected and there was no liver present. This system was able to record the fact that this segment of the liver had been removed.

EXHIBIT 111



Here is still another (exhibit 112) in which there is a single nodule present in the liver. I think you can see the defect very clearly at this point. This proved to be a metastatic lesion, a lesion from the cancer of the lung that had jumped to the liver, it was very helpful in determining that this liver was abnormal and had an area in it that was not liver and was being replaced by some other tissue.

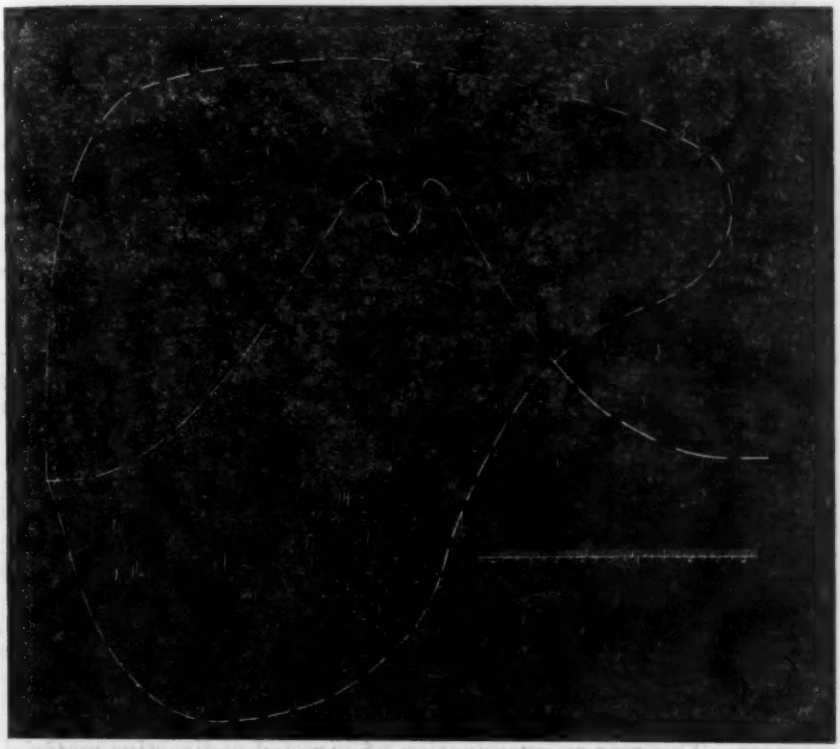
EXHIBIT 112

We have others. Here is just another example (exhibit 113). Just to draw the outline, it may be hard to follow. The left half of liver was replaced by tumor tissue. Therefore, there was no function, and we could clearly see that some important derangement had occurred.

I think this study is very useful for examining livers under these various circumstances. I have others that I could show you. But these are as descriptive as any.

One of the important things, I think, is to differentiate liver from other structures. This often proves to be a fairly important clinical problem. Sometimes we think tissue is liver and actually proves

EXHIBIT 113



not to be liver. This examination helps us a great deal in immediately differentiating liver from nonliver tissue. When the liver is displaced, it is easy to determine this. When the character and morphology has been markedly distorted, as I have shown you here, it is fairly easy to do. So we are pursuing this rather vigorously because we feel that it has a great deal of promise in a field that has been essentially untouched until recently.

This approach can be used in other directions as well. We have already started on the heart. One of the things we can do is to introduce a radioactive material which may be deposited in the vascular system. Occasionally we have problems of looking at the heart by X-ray in trying to decide whether the heart is all muscle or all blood, or whether there is fluid in the sac, which is around the heart. This helps us a great deal because we can now see the blood mass itself, and separate it from the rest of the structure that we see in the heart.

The studies are very early, but they look promising in this direction as well.

One other system that I would like to mention very briefly has to do with the gastrointestinal tract. I would like to discuss briefly some studies that we have done on protein enzymes. Previously in order to study whether there has been any important derangement in protein enzymes, it was necessary to put the patient in the hospital, very carefully put him at basal levels, carefully determine the intake and output of various constituents in his diet, and then make some decision as to whether there was some interference with the enzymes which digest the various food elements. With the use of certain proteins that are tagged with radio elements, it is possible to markedly shorten and circumvent much of this study and make some determination immediately.

This is simply done by taking a protein tagged with radioiodine—this appears to be a very useful isotope—and then determining what happened to the radioiodine. This may be observed from the following:

If the enzymes are plentiful, they will promptly break up the protein and release the iodine itself, or the iodine attached to the soluble segment of this complex molecule. This will promptly disappear into the blood and will come out of the gastrointestinal tract.

If on the other hand these enzymes are low or for some reason are absent, then this complex protein is not broken down, and it will remain in the gastrointestinal tract and not appear in the blood. By making simple studies in this direction, it was possible to show that we could do this.

Here is an example of patients who were known to have pancreatic insufficiencies (exhibit 114), and I think you can see very marked differences. This was an examination of ingested radioactive material in the stool. This makes stool studies very simple, because it is not necessary to do any complex chemical analysis. You simply take the material and place it in a jar next to a counter, and it is very easy to record.

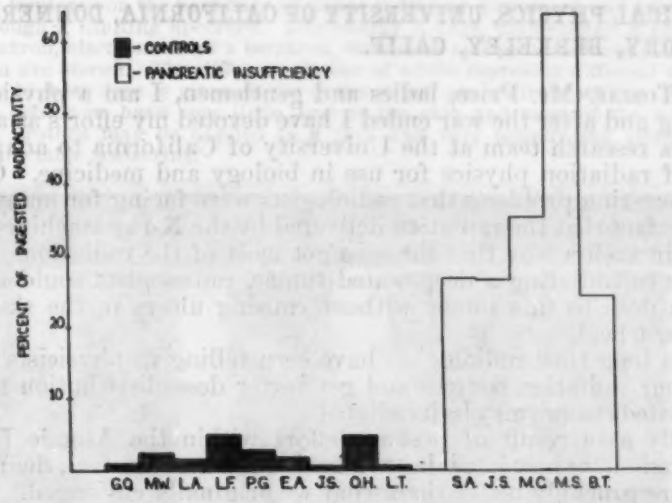
You can see that the controls showed that there was very little present in the excreta, because they were able to break down the protein and absorb it very promptly. Whereas in the large white area you can see that a large amount remained for the reason that they had a serious impairment of the protolytic enzymes, and were therefore unable to break down and absorb it.

Before I finish, I would like to just make one more reference to some new work that has been done by a colleague of ours at the University of California, Dr. Taplin, who has done some very interesting studies on determining the function of the liver and the kidney.

May I have the first slide? This is a typical curve he has published, and is based on the fact that the rose bengal is metabolized by the liver and may be tagged by radioiodine for ready detection. By placing the counter directly over the liver, you can determine whether the dye has been properly taken up by the liver, and how it is remaining in the liver.

Here he has drawn these curves. Here is a normal. Here is a case of acute hepatitis, showing that it has difficulty taking up the tagged liver dye and handling it, and is backing up someplace else.

EXHIBIT 114



Here is a case of chronic liver disease, with marked impairment of function and you can see it does not have a normal peak and remains at a constant low level.

Here we can see a comparatively simple and immediate study that can be made on liver function, and may easily replace the previous studies that have been made with this material. Previous studies would involve actual sampling of the blood and studies of the excreta in order to determine the disappearance of this material from the bloodstream, and its handling by the liver. These curves are to the clinician very helpful in making an immediate decision about liver function.

He has done the same thing in kidney diseases. It is possible to take compounds which are ordinarily excreted by the kidney and tag them with a radio element. Then it is possible to make measurements over the kidney tissue proper by simply placing a counter over the kidney.

Here he has some examples. This is a normal curve. There is the appearance of the curve when there is a complete obstruction of the urinary flow by a stone which is present. The urine, therefore, cannot flow. This material then enters with great difficulty. Then you look at this afterward, 2 months after the removal of the stone, you can see that there has been a marked reversal from this curve, and it shows clearly that there has been improvement in the way that the kidney handles this compound.

I think this is all I want to say. I hope that this gives you some concept of how we can apply these problems.

Representative PRICE. It certainly does, Doctor. We appreciate your presentation here this morning. Thank you very much.

Dr. ALBERT. The next speaker is Dr. Cornelius Anthony Tobias. He will talk on the medical uses of high-energy particle accelerators.

STATEMENT OF DR. CORNELIUS ANTHONY TOBIAS, PROFESSOR OF MEDICAL PHYSICS, UNIVERSITY OF CALIFORNIA, DONNER LABORATORY, BERKELEY, CALIF.

Dr. TOBIAS. Mr. Price, ladies and gentlemen, I am a physicist by training and after the war ended I have devoted my efforts as a member of a research team at the University of California to adapt new tools of radiation physics for use in biology and medicine. One of the interesting problems that radiologists were facing for many years was the fact that the radiation delivered by the X-ray machines penetrated in such a way that the skin got most of the radiation. When it came to radiating a deep-seated tumor, radiologists could not get enough dose to this tumor without causing ulcers in the skin that would not heal.

For a long time radiologists have been telling us physicists to improve our radiation sources and get better dose distribution so that deep-seated tumors may be irradiated.

Chiefly as a result of postwar effort within the Atomic Energy Commission, we now have these radiation sources. In fact, their properties are probably better than what we originally envisaged.

I shall show a chart (exhibit 115) which summarizes the physical properties of these sources that relate to the medical use.

There are too many kinds of radiation sources actually for me to have them all on this chart. The different painted areas indicate how the radiation dose is delivered deep inside of the tissue when a beam of 1 inch in diameter is directed perpendicularly to the surface of the skin which is indicated by the horizontal line. The conventional X-rays deliver most of the dose up at the skin where the graph is painted white, and then the dose decreases by absorption deeper in tissue.

The second example I am showing is due to the X-rays from a betatron of 25 million volts. Here you can clearly see that the maximum dose delivered is more than an inch below the surface, and then the radiation gets absorbed slowly. Also, sidewise there is less scattering. The areas that would be away from the area that we wish to radiate would get less radiation in effect.

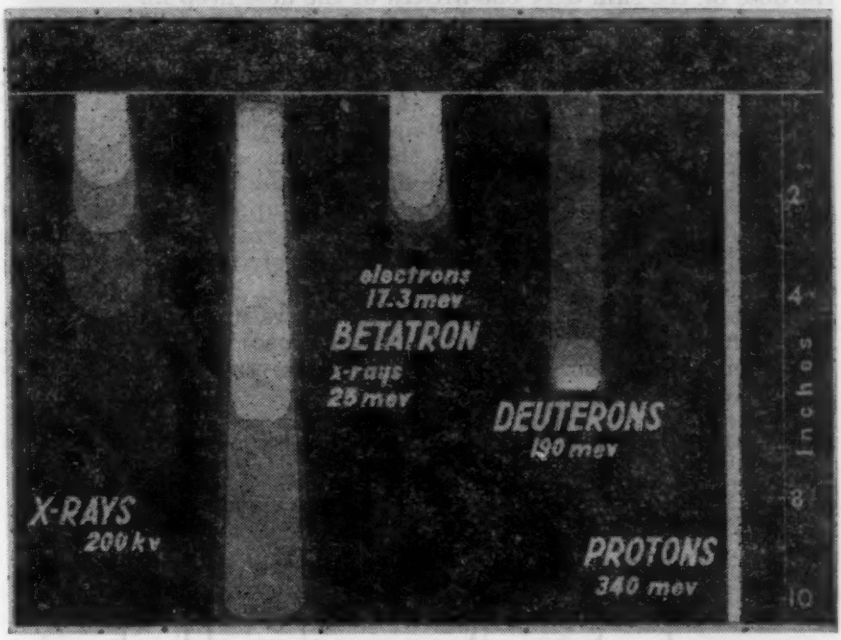
The third dose distribution is due to electrons from a betatron. The electrons are accelerated inside and are deflected out by special methods. This radiation is particularly good when we do want to irradiate a layer under the skin and deliver a big dose there, and have the beam stopped before it penetrates too deeply so that the deeper radiation-sensitive areas would not be affected.

Representative PRICE. Just for purposes of clarification, Doctor, your radiation is being beamed from the top side of that line?

Dr. TOBIAS. Yes; it is being beamed down. It is limited by some sore of aperture to the size shown, 1-inch diameter.

I have been engaged for the last 6 years in work with the 184-inch cyclotron at Berkeley. The deflected beams from this machine have for some purposes even more interesting dose distribution than the previous ones shown. Two examples of that are shown here. One of them is a case of the 190-million-volt deuteron radiation. These are the nuclei of heavy hydrogen. As they penetrate into the body they have only small effect on the skin most of the way in, for a path

EXHIBIT 115. Relief map of dose distribution from various radiations. Each ray impinges on the boundary of tissue radiating downward and having passed through a limiting aperture. Low-energy X-rays, high-energy X-rays from a betatron, electrons from a betatron, deuterons and protons from a large cyclotron are shown. The different shades of white represent different dose rates. The highest dose is given in the areas which are entirely white. Notice that the deuterons have very little dose at the skin and most of the way in, and the protons may be applied in a thin and very penetrating pencil without appreciable scattering.



of about 5 inches. Near the end of the path of the ions rather suddenly the dose increases sharply, and then within a very short distance the beam completely stops. So you can direct this radiation against any spot deep in tissue that you may want to irradiate if you know the desired location and depth.

You can adjust the range of the deuteron ions by placing suitable absorbers between accelerator and human body and then delivering a tremendous dose inside. We deliver four times as much dose at the maximum point than on the skin.

Senator PASTORE. How do you do that? What is it that you do that brings the force down way deep in the body?

Dr. TOBIAS. We accelerate heavy hydrogen particles in a cyclotron up to 190 million volts energy. When their velocity is near to that of the speed of light they have the property to interact only to a small degree with tissue as long as they go fast. The tissue slows the particles down and when they go slow, they interact very strongly. So more dose is produced just before the particles are stopped.

Senator PASTORE. I don't know whether or not I am competent to ask the question, and whether or not you would care to answer it, but how would you line this up with the difficulty that was expressed here a short while ago by Dr. Sweet, with reference to these severe

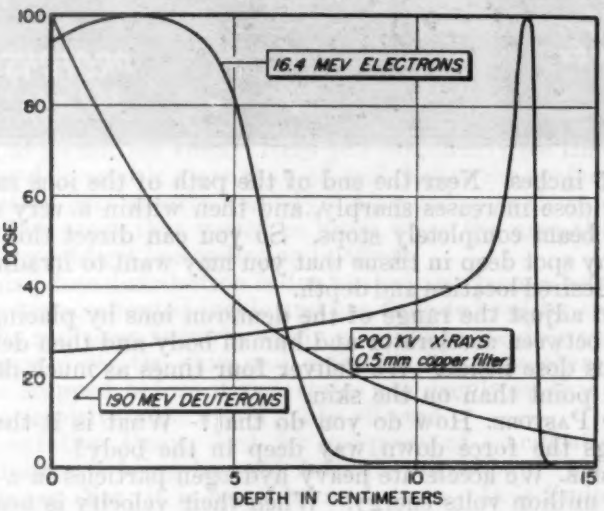
burns on the outside of the skull with reference to the treatment of brain tumors? Isn't that in the direction of finding an answer to our problem?

Dr. TOBIAS. Exactly, Senator. The heavy-particle beam allows a method of irradiation whereby we do not burn the skin at all, and yet are able to radiate any volume inside with almost any dose we desire. In fact, in some applications I will show later, we can have the dose on the skin only one-fiftieth of the dose deep in.

The last dose distribution shown is from protons. These are the nuclei of hydrogen atoms of 340 million volts accelerated in the big cyclotron. These have the property of penetrating very deeply. They could in fact almost cross an elephant. They do not scatter appreciably nor diminish in intensity. They might be regarded as a straight pencil of radiation that may have uniform biological effect all along its track. The diameter of the beam may be made as small as a sixteenth of an inch. So if we apply this radiation in a so-called multiple-port fashion by radiating from several directions to the same point in a body we can get extremely high doses to a very small region inside.

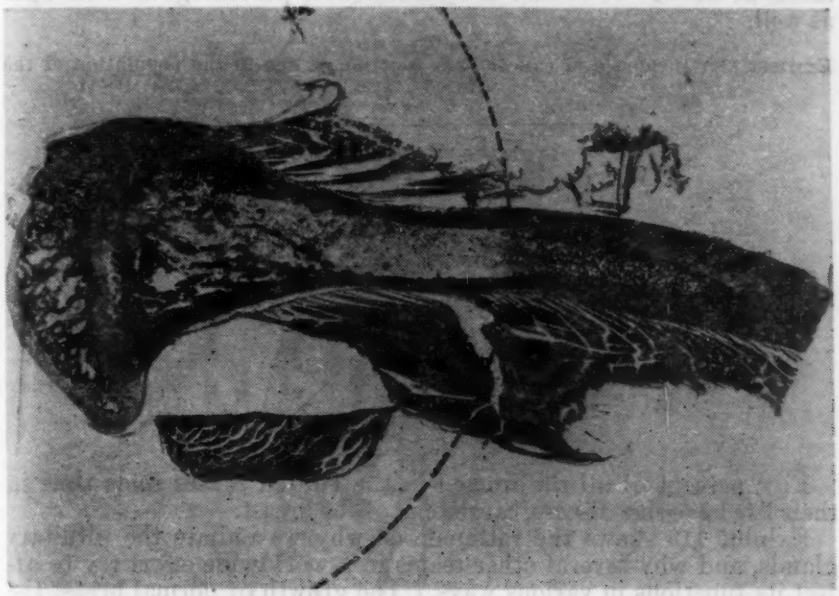
May I have exhibit 116. This exhibit shows in more quantitative fashion how the ionization of the X-rays decreases with depth and that of deuterons increasing and coming up to a very sharp peak deep inside living tissue.

EXHIBIT 116. The dose as a function of depth of penetration in tissue is shown for 200 kilovolt X-rays, 16.4 Mev. electrons and 190 Mev. deutrons.



In exhibit 117 we see that the proton beam behaves almost like a surgical tool. Here is the bone of a rat. The knee joint was radiated as shown on the figure by the dotted lines of the boundary of the radiation field. The histological section was prepared 4 weeks later. To the left of the boundary line the bone marrow completely disappeared. On the right of the line it is alive and normal. The demarcation line is as sharp as you can make it with a knife.

EXHIBIT 117. Historical section of rat tibia 36 days after deuteron irradiation. The boundary of the beam is shown with dotted lines. To the left where the bone received 2,000 roentgen the bone marrow is depleted from cells and severe radiation damage is apparent. To the right there is normal bone marrow indicating that the microscopic demarcation line exists between radiated and nonradiated portions. Magnification 140 times. Slide courtesy of Professor Rhinehart.



From the above examples, you can see that we now have the visible tools available to produce almost any dose distribution inside the body, and a number of teams in the country are engaged in the obvious effort of treating the actual deep-seated tumors by the various beams available.

However, difficulties arise with such therapeutic efforts: despite the great advances made in diagnosis of the site of tumors, we still are uncertain of their exact location. In order to apply such a fine tool as the cyclotron, we have to know exactly where we want to direct the radiation. So we felt at Berkeley that the direct radiation therapy is not the only answer that we can get by use of our very powerful radiation sources, but we can use this radiation more as an analytic tool or a tool to influence the whole body metabolism.

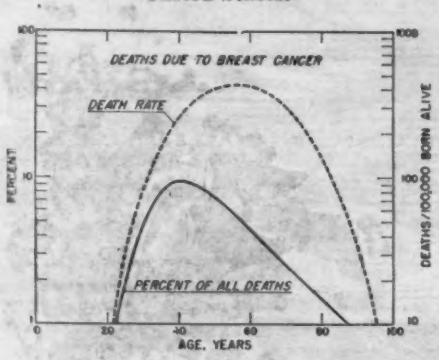
In the next part of this presentation I shall illustrate how we can approach the problem of cancer by use of irradiation by indirect methods. In order to indicate the rationale behind our efforts, I should mention that it is now known that the growth and origin of many tumors in human beings and in animals is intimately related to the functions of the pituitary gland. Since the proton and deuteron beams available to us have the wonderful property of being able to affect the small gland inside of the body while leaving other tissues relatively protected, our effort is now directed to radiating the pituitary gland.

I shall have to limit myself to one kind of cancer, and that is breast cancer, which is a very serious disease, causing mortality in the population of the United States. In the current year, 20,000 people, 99 per-

cent of them women, are expected to die from this disease, and perhaps 3 to 5 times as many, or around 80,000 people, actually currently suffer from this dreaded disease.

Exhibit 118 shows the mortality, from cancer of the breast, which is as much as 10 percent of the mortality of the population of the females at the age of 40 and is a considerable percentage at later ages as well.

EXHIBIT 118. Incidence of cancer as a function of age in the population of the United States.



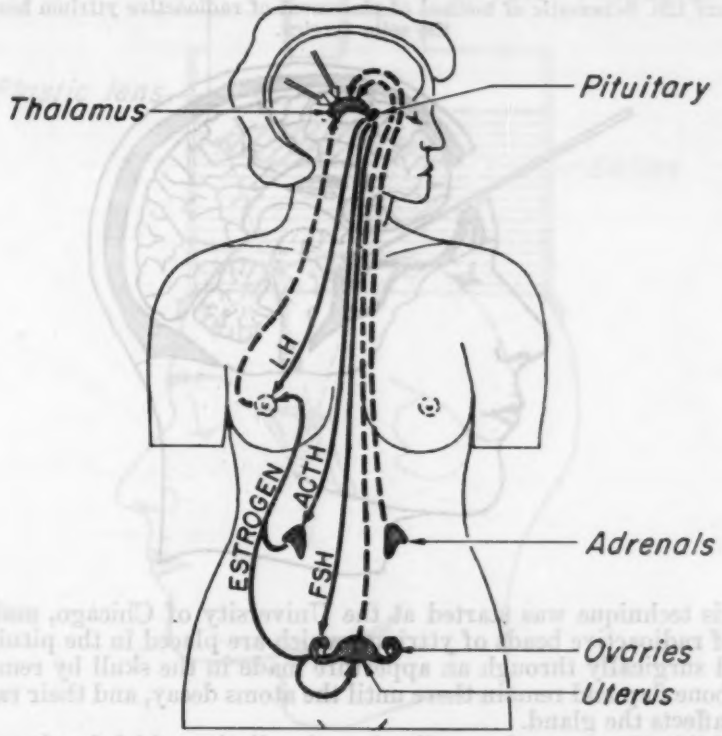
Five percent of all the women in the United States some time in their life have this disease, carcinoma of the breast.

Exhibit 119 shows the rationale of why we radiate the pituitary glands, and why several other teams in a worldwide effort try to affect its functions in various ways. The growth of normal breast tissues is essentially controlled by hormones of the master gland, that is, the pituitary. They are controlled in a very complicated way, and exhibit 119 is only a simplified diagram. Among the factors involved are the pituitary gonadotrophic hormones affecting the growth and function of the ovaries. The ovaries in turn pour out estrogenic substances, which will cause the breast tissue to grow. Another hormone of the pituitary has a direct effect producing lactation, or mother's milk. There are probably still other hormones that regulate the growth of normal breast tissue. A curious feedback arrangement exists which is indicated by the ascending lines of figure 5. To a physicist the hormonal functions of the body are regulated very much like in an automatic controlling machine. Messages are sent up to the hypothalamus as to how much hormone should be secreted, and this nerve center appears to transmit the information to the pituitary, resulting in a change of secreted hormone levels.

According to present knowledge, the hormones of the pituitary may be essential for the growth of carcinoma of breast, in perhaps 40 or 50 per cent of all cases. I don't have time to go into all the evidence, but I might mention that estrogenic substances have caused breast cancer in several species of animals when administered. They have even caused breast cancer in the castrated male mice.

Androgenic (male hormonal) substances which counteract estrogens have been used therapeutically for several years, and give relief from

EXHIBIT 119. Schematic of hormonal control of breast tissue. Pituitary gonadotropins affect the ovaries and adrenals which in turn produce estrogenic substances. These and the lactogenic hormone and perhaps other pituitary hormones cause breast tissue to grow. The dotted lines show a feedback mechanism of control which acts through the hypothalamus.



breast cancer sometimes lasting for several months. For about 15 years an operation involving removal of ovaries (oophorectomy) has been practiced, which may give regression or relief from the disease lasting for perhaps a year. For the past 10 years, due to the efforts of Professor Huggins of the University of Chicago and our present associate, the adrenal glands could be taken out surgically, and the adrenal glands are also known to produce some of the essential female hormonal substances. It seems that for some people this affords relief from symptoms of breast cancer for about 2 years. However, after this period the disease seemed to return. People began to suspect the pituitary since, even in the absence of these so-called target organs, the ovaries and adrenals, the pituitary or master gland is still present putting out all the main classes of hormones.

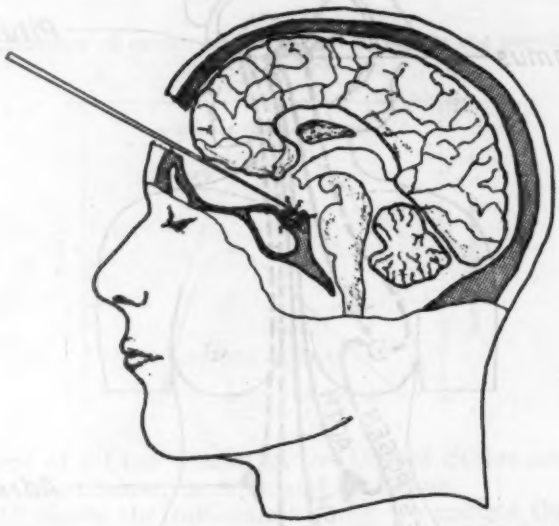
In 1952 Professor Olivecroma et al. in Sweden and Perrault et al. in France for the first time successfully operated on patients with breast cancer by removing their pituitary glands entirely and some striking remissions resulted.

At the present time in the United States great efforts are being made to remove the pituitary gland of human beings suffering from breast cancer by surgery and radiation. The surgical problem is a

very difficult one because the gland is located right in the middle of the most sensitive structures of the brain. The radiation approaches are several, and I shall very briefly show some of them.

One approach is shown on exhibit 120.

EXHIBIT 120. Schematic of method of placement of radioactive yttrium beads in the sella turcica.



This technique was started at the University of Chicago, making use of radioactive beads of yttrium, which are placed in the pituitary gland surgically through an apperture made in the skull by removal of a bone flap and remain there until the atoms decay, and their radiation affects the gland.

Exhibit 121 shows the application of radiation which has been not actually tried for pituitary radiation as yet. I am showing a way that might be feasible, based on the work of Dr. Fry, at the University of Illinois. Ultrasonic radiation is allowed to focus in the pituitary after passing through part of the brain. The large bone flap is actually taken off in a surgical operation to allow this procedure. There is serious objection at the moment against the procedure, and that is the reflections from bone which may put a dose in the wrong spot.

The next picture (exhibit 122) shows how we are utilizing the 340 rev. protons in Berkeley. A layout of the big cyclotron is shown. The beam is deflected and it passes through the physics experimental cave, then it continues to the medical cave. So both of the caves can be used simultaneously. The instrument is so precious that we have to arrange it this way. Patients are located in the medical cave with monitor and control equipment outside the shielding.

EXHIBIT 121. A proposed method for ultrasonic radiation of the pituitary gland. Reflections from bone will probably render this method impractical.

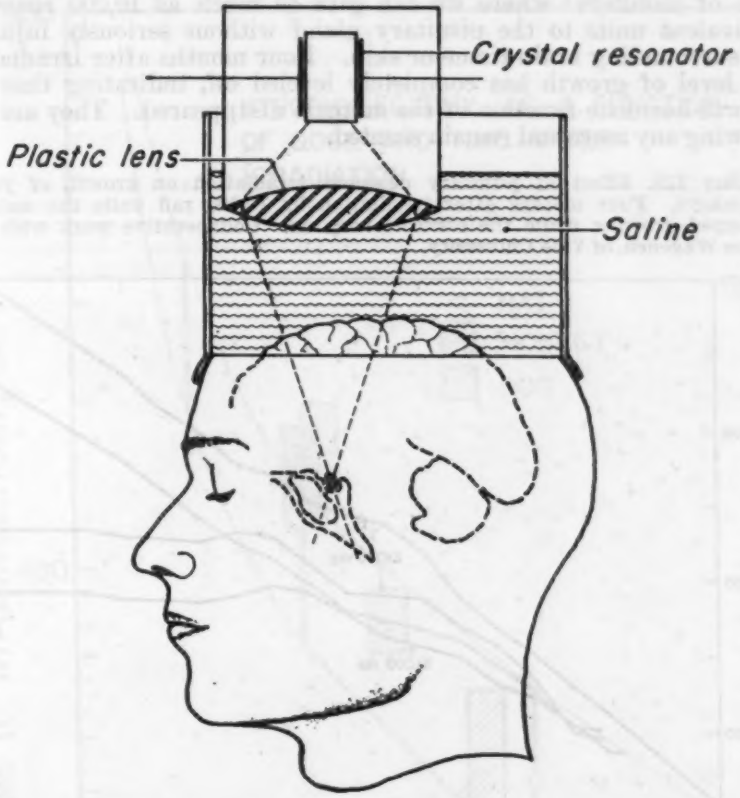


EXHIBIT 122. General layout of the 184-inch cyclotron and the irradiation rooms. The deflected beam passes through a cave for physics experiments and then proceeds to the medical cave.

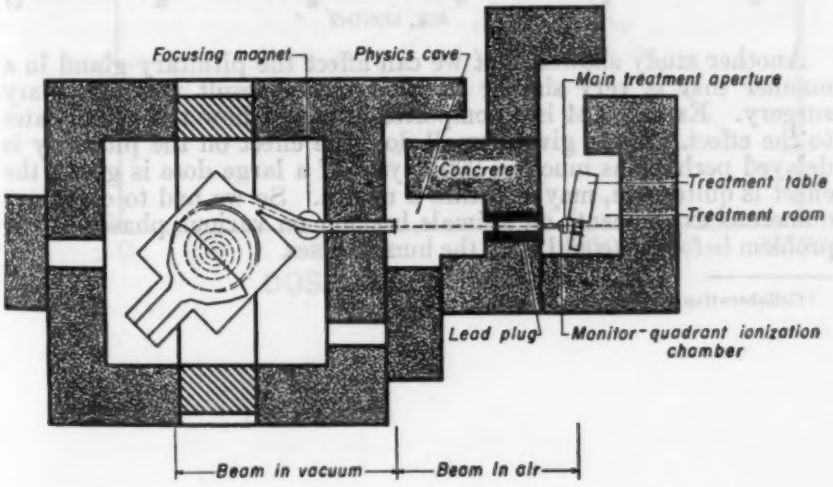
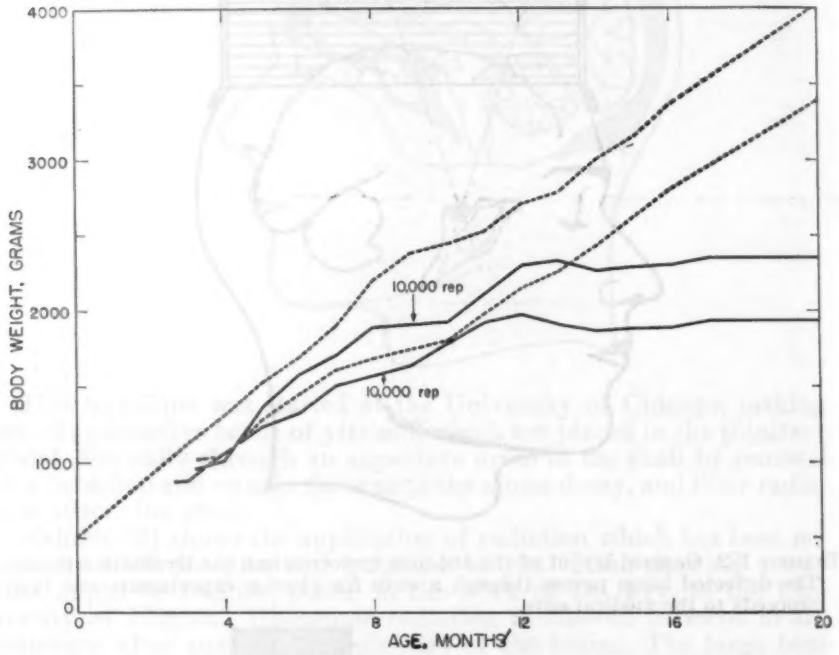


Exhibit 123 shows very briefly what happened when we irradiated the pituitary of animals with deuterons. This is an example in the case of monkeys[1] where we can give as much as 10,000 roentgen equivalent units to the pituitary gland without seriously injuring the surrounding brain tissue or skin. Four months after irradiation the level of growth has completely leveled off, indicating that the growth hormone function of the animals disappeared. They are not growing any more and remain stunted.

EXHIBIT 123. Effect of pituitary deuteron irradiation on growth of young monkeys. Four months after irradiation by 10,000 rad units the animals stopped growing while the controls keep on. Collaborative work with Dr. Van Wagenen, of Yale University.



Another study showed that we can affect the pituitary gland in a manner that is very similar to what might result from pituitary surgery. Exhibit 124 is a composite graph of how the dose relates to the effect. If we give a small dose the effect on the pituitary is delayed perhaps as much as 200 days. If a large dose is given, the effect is quite soon, maybe within a month. So we had to carry out numerous experiments on animals bearing on various phases of the problem before we could go to the human cases.

[1] Collaborative project with Yale University.

EXHIBIT 124. Dose time relationship for effects of protons and deuterons on pituitary function. The effects of a higher dose appear sooner.

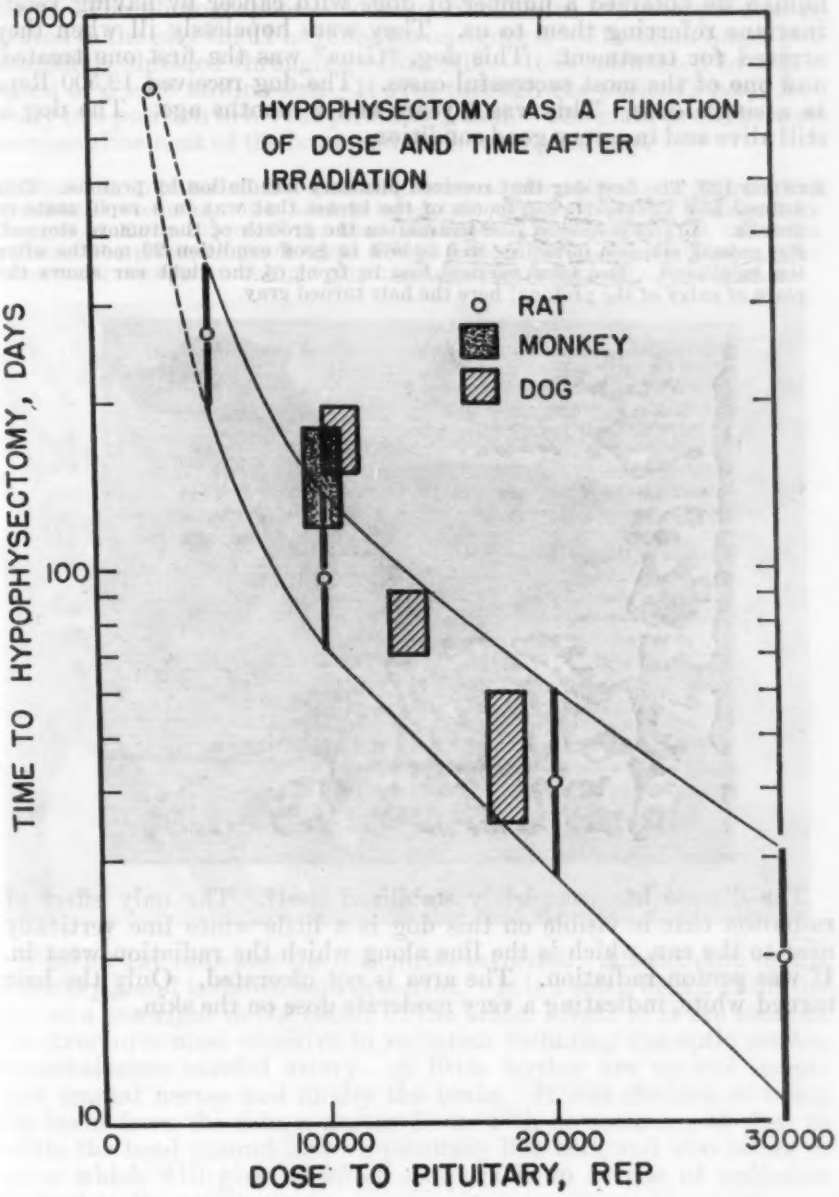
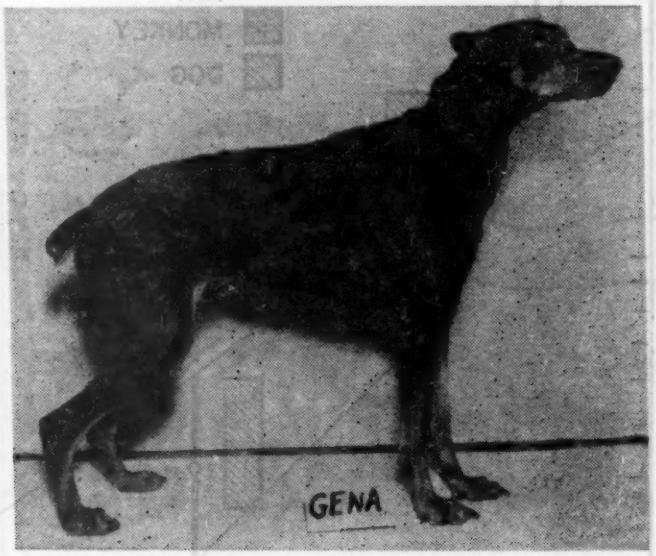


Exhibit 125 then shows the next stage in this work. Many dogs have spontaneous mammary cancer. Before trying the beam on a human we obtained a number of dogs with cancer by having veterinarians referring them to us. They were hopelessly ill when they arrived for treatment. This dog, "Gina" was the first one treated, and one of the most successful cases. The dog received 12,500 Reps in a single dose. This was 2 years and 2 months ago. The dog is still alive and in a very good condition.

EXHIBIT 125. The first dog that received pituitary irradiation by protons. This animal had metastatic carcinoma of the breast that was in a rapid state of growth. In the period of post-irradiation the growth of the tumors stopped, the animal stopped lactating, and is still in good condition 26 months after the treatment. The faint vertical line in front of the right ear shows the place of entry of the protons; here the hair turned gray.



The disease has completely stabilized itself. The only effect of radiation that is visible on this dog is a little white line vertically next to the ear, which is the line along which the radiation went in. It was proton radiation. The area is not ulcerated. Only the hair turned white, indicating a very moderate dose on the skin.

The next picture (exhibit 126) shows the setup which several of us in Berkeley have developed of humane exposure. The patient is lying down. The photographer is looking from above. The apparatus is located in the cave that I have shown on figure 8. The beam comes out completely shielded through an iron tube. It is collimated to a fine pencil of 5 by 8 millimeters. It goes through the patient's head laterally in a position to hit the pituitary gland. The main problem here becomes alinement of the beam and the human pituitary.

EXHIBIT 126. Interior of the treatment room at the 184-inch cyclotron. The patient is reclining. Her head is being held in a rigid plastic mask and by means of X-ray diagnosis the head is placed in such a way that the beam crosses the pituitary gland while avoiding other radiosensitive tissues. The treatment consists of multiple port irradiation and rotation.

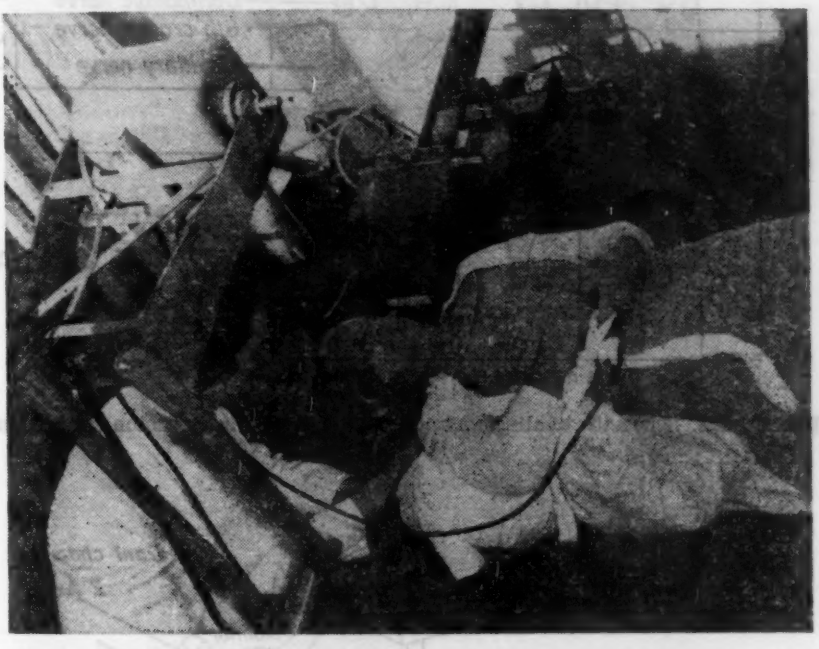


Exhibit 127 indicates the difficulties involved. A schematic of the pituitary gland is shown here in section. It is a small organ about the size of a pea right in the center of the brain. Next to it are some of the structures most sensitive to radiation including the optic nerves, hypothalamus, carotid artery. A little farther are several important cranial nerves and finally the brain. It was decided to bring the beam from the side, a proton beam with no scatter, and then to rotate the head around its own pituitary like this, and also rotate in space which will give an effect comparable to a cone of radiation focused on the pituitary.

EXHIBIT 127. The anatomical detail of the sensitive structures around the pituitary gland. Important nerves are shown that should be protected. The pituitary gland is the kidney-shaped body in the center of the picture.

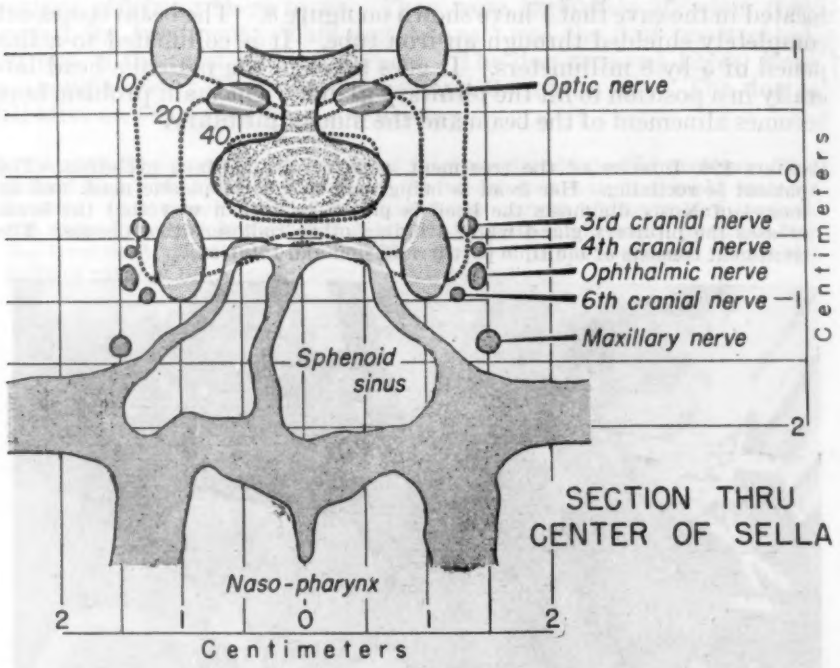


EXHIBIT 128. Schematic of alinement of a patient for pituitary proton irradiation.

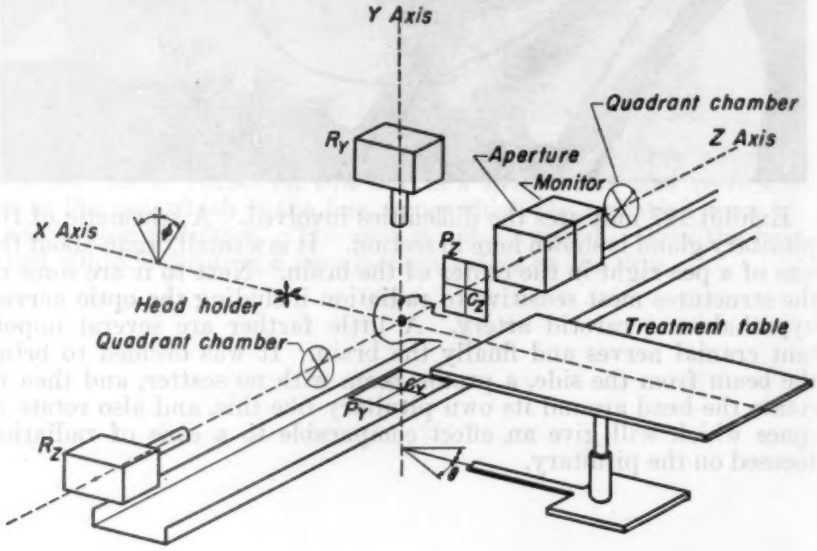


Exhibit 128 shows how the alinement was made. We have to aline the patient with about one-thirty-second of an inch accuracy. Two machines are used for diagnostic purposes. The proton beam is first alined exactly to the axis of the apparatus and by means of diagnostic X-ray films, the patient's pituitary is also alined to be on the same line, and then the vertical X-ray machine helps to aline the center of rotation. X-rays of the sella turcica containing the pituitary gland are shown in exhibit 129.

EXHIBIT 129. In order to aline the pituitary gland, first the sella turcica which contains the gland is brought into alinement with the cross hairs which indicate the position of the beam (upper picture). When the beam is turned on, it fills out the space inside of the sella turcica (bottom picture).

The top picture shows the sella turcica in alinement with the cross hairs. On the lower picture you can see the beam going through the same patient filling out the sella turcica. Of course, we can adjust the size of the beam and vary a number of other factors.

In collaboration with Dr. John Lawrence, director of the Donner Laboratory, and a number of other medical experts, including the late B. V. Low Beer, we started in September 1954 to give pituitary proton radiation to a number of very advanced cases of metastatic carcinoma of the breast. The criterion was that the patient should have had all other available therapy, so most of these patients had previous mas-

tectomy operations, X-rays, their ovaries and adrenals removed, and objective evidence was available to the effect that the disease was progressing with no hope for arrest.

The study is only in its second year now, and we might say that we have only made a beginning in a very complex undertaking. We have really three objectives in this study. First, we wished to show that we can produce by protons a state of hypophysectomy which was never attained previously by any kind of radiation.

Secondly, we wished to show the magnitude of the radiation effect on the brain, and show that the brain and the rest of the tissues were not unduly affected. Previously protons were never used in human irradiation studies.

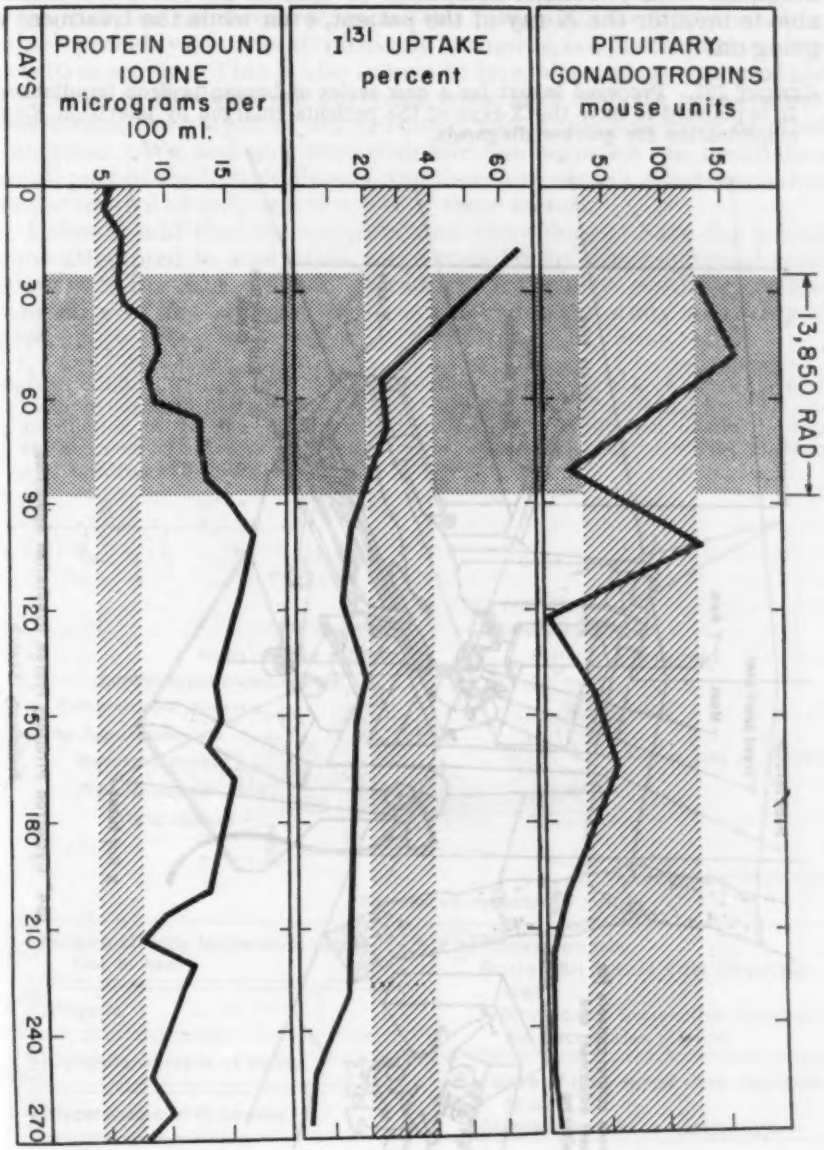
Third is the effect on the tumors themselves. I can report today that the first two objectives seem to be fairly well attained, a gratifying situation in view of the shortness of the time. We can produce a physiological state in the human corresponding to phyophysectomy. Pathologically, 95 percent or more of the hormone producing cells disappear. Any cells that remain there probably do not function normally. Physiologically by testing the thyroid gland, we can show that in all patients the functions of the thyroid gland are greatly reduced, and in some cases seem to be completely absent so that they need supporting thyroid extract.

The sex hormone output, which is measured in the urine of these patients, goes down in many of them to a level where it is not measable any more.

Exhibit 130 shows the results of some physiological measurements in one patient. The pituitary gonad tropines are very high previous to radiation and they go down and stay down at a low level following it. The thyroid function is measured by the uptake of radioactive iodine. In this patient it started quite high and progressed to a low level. The study has only been progressing for approximately 2 years and so far 26 mammary cancer patients have been irradiated. Many other physiological tests are being carried out simultaneously to obtain more knowledge of the hypophysectomised state.

It is too early to bring you a complete report as to the extent of benefit that a large number of cancer cases would receive from pituitary proton therapy. However, the results on the early cases gave us a certain amount of encouragement, to the extent that we plan to irradiate a number of additional patients, probably at least 100 in number in the near future, to find out objectively what the place of proton pituitary therapy among the treatments of breast cancer will be.

EXHIBIT 130. Typical physiological changes due to pituitary irradiation. Top graph shows the decrease of sex hormone in the urine of patients to a level which indicates lack of function of the pituitary gland. In the center graph is the uptake of radioactive iodine in the thyroid gland. This also decreases to low levels.



At the moment the cyclotron is being rebuilt as it will be changed over to higher energy. Exhibit 131 shows a new device now being built for work with patients, which is like the one we used before, except that it will accelerate the work by combining the actual X-ray diagnosis with television equipment so that at all times we will be able to monitor the X-ray of the patient, even while the treatment is going on.

EXHIBIT 131. Proposed layout for a new series of human protron irradiations. It is planned to have the X-rays of the patients enlarged by television X-ray amplification for quicker diagnosis.

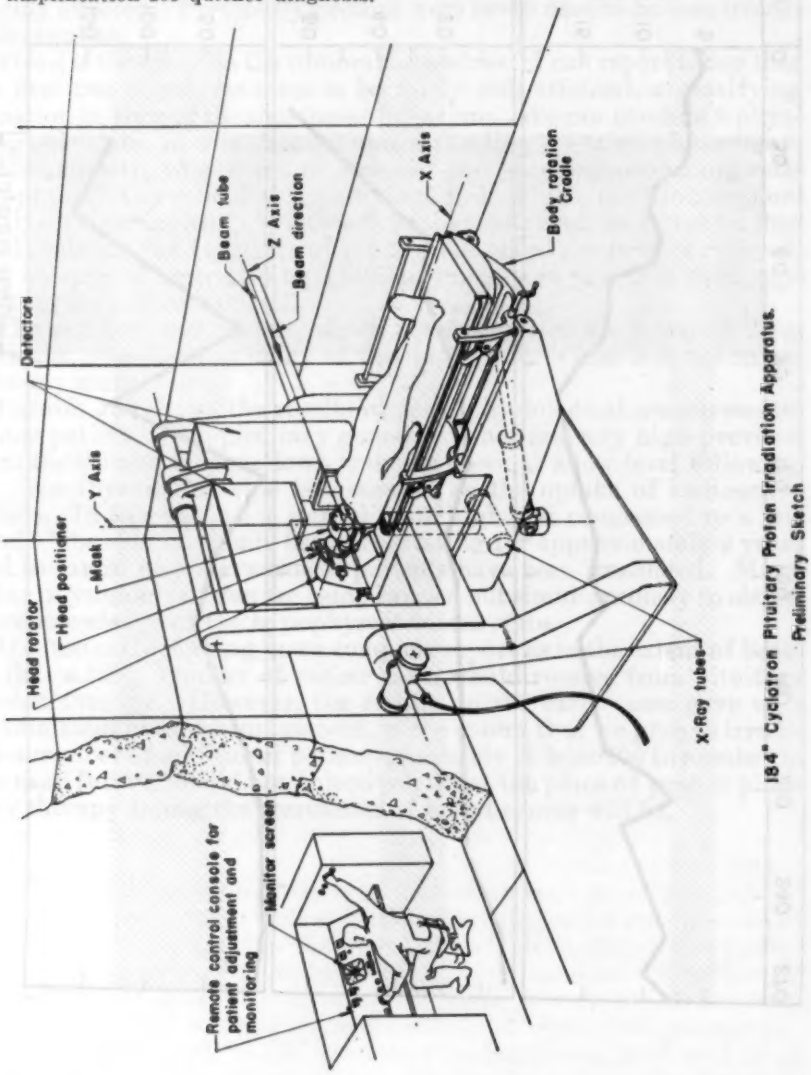
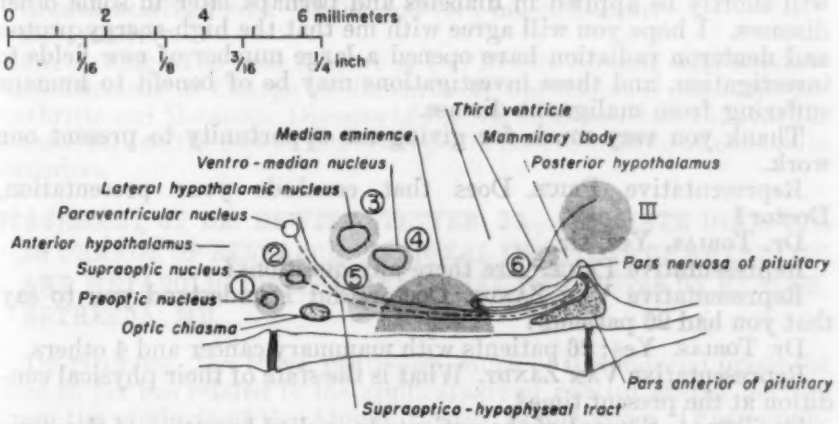


Exhibit 132, which is the last one, shows where the work with small animals, rats, is progressing. While the pituitary therapeutic radiations are going on in the humans we are attempting to make basic explorations in small animals that may point to future beneficial human uses. It was found out by controlling the location of proton dose that the nerve center above the pituitary, the hypothalamus, which probably controls all pituitary hormones, is a particularly radiosensitive region. This is also known to be a place where many of the functions of the body are governed from, such as body temperature, heart rate, the output of sex hormone, and a large number of other functions. We find now that with our fine beam we can irradiate a small part of the hypothalamus, and therefore cause a selective change in the control of only one or a few of these factors.

I should add that the surgeons and physiologists have for a long time attempted to study this nerve complex by direct surgical techniques. This is a difficult procedure, frequently resulting in the mortality of the animals, whereas the radiation study mortality is zero.

EXHIBIT 132. Locations in the hypothalamus where control of pituitary hormone production has been established. By means of irradiating area III the production of growth hormone is impaired and irradiation of the median eminence causes increased water turnover, abnormal carbohydrate metabolism, and abnormal thyroid function.



1. Failure of body temperature regulation to heat.
2. Polyuria.
3. Complete absence of eating.
4. Hyperphagia with obesity.
5. Gonadal atrophy.
   Blocks TSH release after propylthiouracil.
   Interruption of Supraoptico-hypophyseal tract causes polyuria.
6. Failure of body temperature regulation to cold.
   Stimulation leads to hyperphagia.

Exhibit 132 gives a composite chart of the rat hypothalamus, showing how these various areas are geometrically arranged. This graph is an indication, too, how much we may learn in the future by research of this type. We have irradiated several of the indicated areas by small pencils of beam. Here is one area for which previous knowledge was not available.

Injury to the area right above the pituitary acts on the growth of the animal inasmuch as it stops the production of the growth hormone in the pituitary gland.

Injury in another area near the median eminence causes a symptom complex whereby the animal becomes very thirsty. It will interfere with his water metabolism. It will interfere with the functions of the thyroid gland, and the way the body is able to utilize carbohydrates.

We have also been able to obtain animals that become unusually obese after hypothalamic radiation, and occasional ones which develop exophtalmus. I think these samples show you that there is a great deal more to be found out by detailed investigation by means of the proton radiation, and almost each of the body functions I have mentioned has an important role in our well being, their malfunctions relate some way in certain diseases.

To go back to mammary cancer now, if we could find which of the hormones are exactly responsible during the period of the development of the disease, in the future it may be possible to affect with protons the area not in the pituitary gland, but in the hypothalamus, and thus bring about a corrective change.

In summary I have demonstrated to you the properties of high-energy proton beams, the work on the patients by pituitary proton irradiation which is now used on advanced cases of breast cancer, and will shortly be applied in diabetes and perhaps later in some other diseases. I hope you will agree with me that the high-energy proton and deuteron radiation have opened a large number of new fields to investigation, and these investigations may be of benefit to humans suffering from malignant disease.

Thank you very much for giving me opportunity to present our work.

Representative PRICE. Does that conclude your presentation, Doctor?

Dr. TOBIAS. Yes, sir.

Representative PRICE. Are there any questions?

Representative VAN ZANDT. Doctor, did I undestand you to say that you had 26 patients?

Dr. TOBIAS. Yes; 26 patients with mammary cancer and 4 others.

Representative VAN ZANDT. What is the state of their physical condition at the present time?

Dr. TOBIAS. Several of the patients have died but some of them are still alive. I would rather not, in a detailed way, report on this, because we feel that the study is not finished, and we would not want to give the impression either that the treatment is very good or that it is very bad. We know now that we can produce remissions such as are being produced in surgery. What we do not know is what percentage of the cases would get these remissions and how long they will last. I think the people involved in this project are enthusiastic to the extent that we feel that we are learning while we also may benefit some of the people. Perhaps 3 to 5 years from now we will be able to give you a very complete statement regarding the value of pituitary proton therapy.

Representative VAN ZANDT. Have you prolonged the life of any of these people for any number of days?

Dr. TOBIAS. This is a difficult question to answer. We cannot actually predict the life span of any one patient. Therefore, we do not know this. But several of the patients are still alive.

Representative VAN ZANDT. They were acute cases when you received them?

Dr. TOBIAS. All the cases were cases that all other medical science had given up. They were progressing. I may illustrate it in this way. Actually, there was a total of 34 cases accepted for treatment. Four of them died during the week before they could be brought to the beam. One of the 30 remaining patients died during the first week of treatment before the radiation effect could take hold. However, on the other side of the scale, the patient who has lived longest has lived about 17 months since treatment and is still doing well. But still I think we have to be very cautious about being optimistic, particularly since the daily press and some irresponsible people sometimes make statements that may cause false hopes to thousands of suffering people. I think the only objective method of evaluation is by statistics. Since we are aiming for prolongation of life, not in terms of days but in terms of years, it follows that we have to wait for several more years before the therapeutic value is fully assessed. On the other hand, I can only say that several members of our group are encouraged by the preliminary studies, and we are trying to get the answers as fast as we can.

Representative PRICE. Thank you very much, Doctor.

Dr. Albert?

Dr. ALBERT. The next speaker is Dr. Dewitt Stetten, who is Associate Director in Charge of Research at the National Institute for Arthritic and Metabolic Diseases of the National Institutes of Health. He will talk on the uses of radioisotopes in the elucidation of metabolic disorders.

STATEMENT OF DR. DEWITT STETTEN, JR., ASSOCIATE DIRECTOR IN CHARGE OF RESEARCH, NATIONAL INSTITUTE OF ARTHRITIC AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MD.

Dr. STETTEN. Mr. Price, gentlemen, much of the material presented here so far has related to the applications of radiant energy derived from the products of the Atomic Energy Commission. Other applications have been touched on and these I should like to discuss a little more fully, namely, the use of atoms themselves as tracers for the measurement of processes which occur in biological systems.

In the intact animal or human body, a large number of chemical transformations are occurring simultaneously and more or less continuously. By these reactions the organism accomplishes several ends necessary for continued life. It generates from its nutrients and from its tissues the compounds which it requires. It liberates from the constituents of the diet the energy to provide for the numerous energy-requiring processes of the body. It transforms unneeded wastes into a condition suitable for excretion. It preserves the complex architecture of the organism as a whole, and offsets the spontaneous disruption and decay which, if unopposed, leads to tissue death.

The reasons why the biologists and the physician are driven to try to understand these chemical transformations are many. Perhaps the most compelling is the fact that no investigator worthy of the name rests entirely comfortably when faced by an unanswered question. Beyond this driving force is the recognition that any biological fact securely establishd must ultimately lead to practical benefits.

Whereas medical advances in the past have been in many instances empirical, more and more we witness today a rational approach to medical science. New discovery is based upon previously established fact. It becomes increasingly important to understand the workings of the organism if we are to understand, diagnose, treat, or prevent disease of the organism. In virtually all diseased states the chemical transformations which I have just mentioned deviate in one or more regards from normal.

It is not surprising, therefore, that a large fraction of the effort in today's medical research is directed toward the study of these chemical reactions in normal and diseased animals and human subjects, the study which is called intermediary metabolism. An enormous interest in this study has stemmed from the availability to medical science of isotopes. First the stable isotopes in 1932, deuterium, soon followed by nitrogen 15 and carbon 13, then the cyclotron products, phosphorus 32 and carbon 11, and finally the products of the atomic reactor, including radioactive isotopic siblings of all the important elements, have been seized upon by biologists and physicians.

Their applications to medical and biochemical problems have become so widespread that perhaps one half of the contributions to the biochemical literature today describe experiments in which isotopes have featured.

The appearance of isotopes on the biochemical horizon was indeed fortunate. Prior to that event, the methods of research in this area all suffered from serious, seemingly insuperable drawbacks. The favored approach was that of analysis, of dissection. The complexities of the organized biological system were circumvented by breaking it apart, first anatomically, then chemically. Much was learned of the chemical composition of the body. The occurrence of many reactions in the body was studied, and the enzymes which catalyze these reactions were characterized, and in many cases purified. Although this method was, and still is, both widely applied and useful, it always leaves an important question unanswered, to wit: to what extent did the experimental procedure influence the process under investigation? To what extent has the reaction, observed in the dissected, disorganized fragment, a counterpart in the intact, highly organized whole, which is the mammalian organism.

This question previously was tentatively answered by a procedure called the balance experiment. To the intact animal a substance was administered and changes in the composition of the tissues and excreta were sought. This method has the advantage of treating with the intact animal but suffers in turn from another defect. One could never be sure that the product observed to increase abnormally after administration of a precursor was indeed directly derived from that precursor. This defect was clearly pointed out by an elderly visitor in our laboratories in the late 1930's, who likened the balance experiment to a slot machine. He said in essence, "I place a penny in the

slot, out comes chewing gum. I therefore infer that chewing gum is made of copper. Repetition of the experiment merely confirms my original conclusion."

The technique of isotopic labeling which made its appearance in the middle 1930's was introduced into biochemistry by Schoenheimer and offered an escape from these dilemmas. By replacing one or more atoms by isotopic siblings in the molecule of a compound of biological interest, the biochemist could prepare a molecule which he could recognize when he met it again. Derivatives and products of such a labeled molecule could also be unambiguously recognizable.

The technique has permitted in many instances the study of a complex series of chemical events in the intact animal while avoiding the pitfall of the classical balance experiment. It should not be assumed that this technique has entirely replaced other experimental approaches. This is not the case nor is it the way of science. What it has done, and this admirably, is to supplement and extend earlier methods of biochemical investigation. Equipped with isotopes of hydrogen, carbon, oxygen, nitrogen, iodine, phosphorus, sulfur, sodium, potassium, iron, and so forth, the biochemist has been able to extend both in scope and in precission his studies of the chemical processes of living organisms.

It would be futile to attempt to review here and now the accomplishments attributable to the development of these materials and the dependent techniques. A very few of these were reported in last summer's International Conference on Peaceful Uses of Atomic Energy at Geneva. It would be more profitable to consider the types of questions which the application of the isotope techniques has answered, and should continue to answer. The scope and power of the method will thus be realized.

The first question is the question of an atomic distribution. We have seen this morning experiments directed toward this end. The question may be phrased, When a compound enters the body where geographically does it go? If the compound bears an isotopic label, one has merely to demonstrate a concentration of isotope at one or another site to answer the question. If the isotope under consideration happens to emit a penetrating gamma ray, as is the case with iodine 131, this can be accomplished, as we have seen this morning, by merely waving a Geiger counter over various parts of the body. If localization at a microscopic level is required, this can be achieved in favorable cases by the application of radioautography, a technique which takes advantage of the properties of radioactive isotopes, and those of photographic emulsions.

The second question can be phrased, Does precursor compound A contribute its atoms to the formation of product compound B in the body? This is the question of the product-precursor relationship. This question is today most eloquently and convincingly answered by the use of isotopes. If the administration of isotopic compound A gives rise to appreciable isotope in compound B, the question is unequivocally answered in the affirmative. By the application of the skills of the organic chemist, it is often possible to synthesize the precursor with isotopes in several different specific locations in the molecule, and also to degrade the product to permit specific assay for isotope in various locations.

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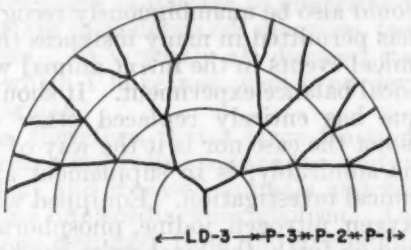
In this fashion an ever-increasing body of knowledge has developed permitting the assignment of a particular atom in a precursor molecule as the contributor of a particular atom in the product molecule.

As an example of this type of research, I should like to present some work recently carried out in our laboratory which will demonstrate some of the points that I have mentioned. May I have the first slide, please? (Exhibit 133.)

EXHIBIT 133



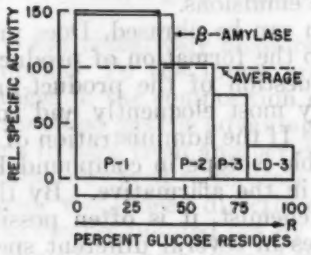
This slide is a diagrammatic presentation of the molecule glycogen, which is a large molecule occurring in the animal body. It is made entirely of glucose residues, linked one to another. The total number in a glycogen molecule ranges from approximately 50,000 to 500,000 glucose residues. It has now been convincingly shown that the pattern in which glucose residues are combined one to another is treelike, a branching pattern shown in the heavy lines on this figure.

The contribution of the enzyme chemists in the last decade have made it possible to dissect this molecule along the lines indicated by the circular marking. One may peel this molecule much as one peels an onion, layer by layer, and they study the contents of each layer.

We have been conducting experiments in which glucose labeled with carbon 14 was administered to animals, glycogen was isolated, the radioactivity in the glycogen measured, and subsequently the glycogen was peeled as is indicated in this diagram.

The next slide (exhibit 134) represents the kind of results we have secured, indicating the radioactivity to be nonuniformly distributed within the glycogen molecule. The highest abundance of radioactivity is found in the outermost layers of the molecule and as one proceeds inward, one encounters lower and lower specific acitivities.

EXHIBIT 134



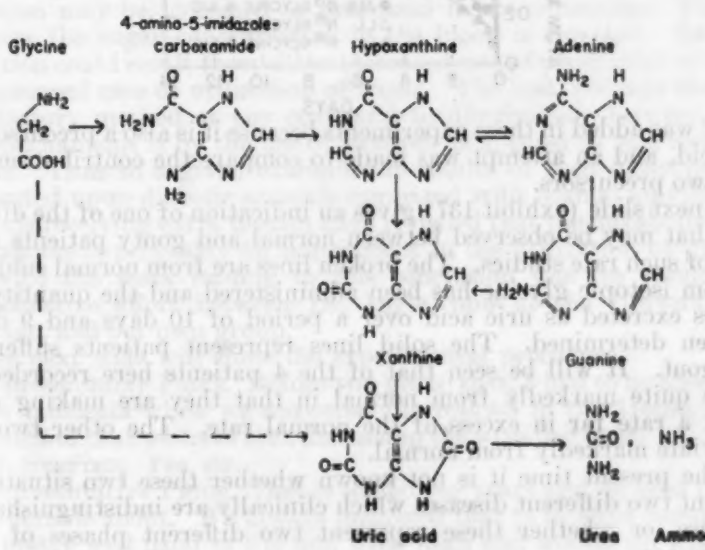
Experiments of this sort have permitted us to reconstruct what was imperfectly understood previously; namely, the mechanism whereby glycogen is synthesized in the intact animal. This type of study, I believe, would have been completely out of the question without the availability of the isotopic labels.

Another question, the third type of question which I should like to consider, is the question of normal rates of body processes. How rapidly is compound A converted into compound B in the animal body? This question was essentially unanswerable prior to the advent of the isotopic technique. Today it may be studied by the measurement of the rate of accrual of isotope in a body constituent, when an isotope precursor of that constituent is administered in trace amounts. Conversely, the same kind of information may be derived from observations of the disappearance of isotope from a body constituent after it has been isotopically labeled by a suitable preliminary procedure.

Studies of this sort have given rise to the now completely orthodox concept of the "dynamic steady state" of certain body constituents. In the normally nourished normal animal, said to be in balance and at constant body weight and constant composition, the several chemical constituents of the body are continuously being broken down and replaced, or are being turned over.

The next slide (exhibit 135) gives the formulas of certain compounds in whose metabolic fate we have been interested. Uric acid is the material which accumulates in the blood and in certain tissues of the body in the disease gout. We know today as a result almost entirely of studies with isotopes, conducted in various laboratories in the country the origin of each of the major atoms in the uric acid molecule. We know what it comes from and how it gets into its appropriate position.

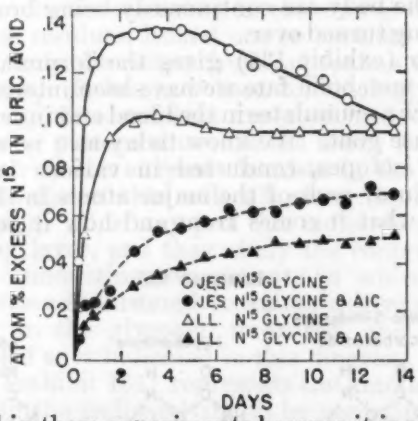
EXHIBIT 135



Among the atoms so considered are those which are known to arise from the amino acid, glycine, a constituent of all proteins and a normal and important component of the normal diet. We have been studying the rate at which the glycine atoms make their appearance in uric acid, in an attempt to find out why in gout there is the increase in uric acid in the fluids of the body which leads ultimately to great deformity and disability in the victims of this disease.

The next slide (exhibit 136) shows the type of data which may be secure. Here are recorded the abundances of isotopes in uric acid found at various times after the administration of isotopically labeled glycine. Two experiments have been conducted on two different subjects. In the course of these studies an essentially accidental finding was made, the exact significance of which is still to be evaluated. It will be noted that the points which are open in both cases fall well above the points which are solid, indicating that the incorporation of glycine into uric acid was quite rapid when nothing else was administered, but was markedly depressed when a material, aminoimidazolcarboxamide (AIC), was added.

EXHIBIT 136

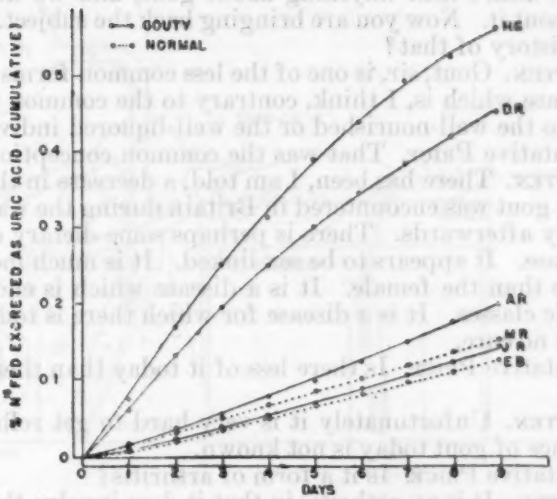


AIC was added in these experiments because it is also a precursor of uric acid, and an attempt was made to compare the contributions of these two precursors.

The next slide (exhibit 137) gives an indication of one of the differences that may be observed between normal and gouty patients as a result of such rate studies. The broken lines are from normal subjects to whom isotopic glycine has been administered and the quantity of isotopes excreted as uric acid over a period of 10 days and 9 days has been determined. The solid lines represent patients suffering from gout. It will be seen that of the 4 patients here recorded, 2 deviate quite markedly from normal in that they are making uric acid at a rate far in excess of the normal rate. The other two do not deviate markedly from normal.

At the present time it is not known whether these two situations represent two different diseases which clinically are indistinguishable otherwise, or whether these represent two different phases of the same disease.

EXHIBIT 137



This, then, is an example of the last type of question which I would like to bring to your attention, the question of how do diseases, administration of drugs, change of diet, surgical procedures, and other stresses, influence the rates of body processes. In seeking the answers to these questions, we are perhaps getting closer to the practical uses of the contributions of atomic energy to medical science. It is becoming increasingly evident that in most or all disease processes there is a metabolic component, a disturbance of the rates of certain chemical processes. The physician is aided by the reports of chemical analyses in his diagnosis. In a given disease some component of blood, tissues or urine, may be increased or decreased in concentration. Thus in diabetes the sugar concentration in the blood is elevated. Such an elevation could result from either increased rate of production of sugar or decreased rate of utilization of sugar. The best, perhaps the only satisfactory method at our command to discriminate between these two mechanisms is by the use of isotopes as applied to rate measurements. Thus in a given example the results of such measurements conducted upon diabetic animals compared with normal animals and animals receiving extra insulin have revealed that the metabolic effect in diabetes is primarily an impairment in the utilization of glucose. Some of the work leading to this conclusion was the result of a collaborative effort between Dr. Ingle, now at the University of Chicago, and our own group.

The next slide will show the experimental procedure.

Representative PRICE. Before you get to that, I had to be absent for a few moments while we answered the rollcall in the House, and I understand that we have been discussing the so-called gout.

Dr. STETTEN. Yes, sir.

Representative PRICE. That is something years ago we used to hear considerable about. We always imagined that to be some person who was pretty well fixed in life and lived high and wound up with that type of ailment. It had become a sort of mark of respectability, I

imagine, or at least some measure of wealth. Then for a long period of time we didn't hear anything about gout, and we didn't see the cartoons about it. Now you are bringing back the subject. Could you trace the history of that?

Dr. STETTEN. Gout, sir, is one of the less common forms of arthritis. It is a disease which is, I think, contrary to the common opinion, not restricted to the well-nourished or the well-liquored individual.

Representative PRICE. That was the common conception years ago.

Dr. STETTEN. There has been, I am told, a decrease in the frequency with which gout was encountered in Britain during the war years, and immediately afterwards. There is perhaps some dietary contribution to this disease. It appears to be sex linked. It is much more frequent in the male than the female. It is a disease which is encountered in all economic classes. It is a disease for which there is today adequate control, but no cure.

Representative PRICE. Is there less of it today than there was years ago?

Dr. STETTEN. Unfortunately it is very hard to get reliable figures. The incidence of gout today is not known.

Representative PRICE. Is it a form of arthritis?

Dr. STETTEN. It is an arthritis in that it does involve the joints and causes painful swelling of the joints. It is a disease which is historically very ancient. As a matter of fact, the treatment of choice today, colchicine, is at least 200 years old, and may stem to ancient Greek medicine. This is still among the most effective treatments.

Representative PRICE. Thank you very much, Doctor. I thought it was an interesting commentary, because we used to hear so much about it, and used to be such a common source of material for cartoonists. This then went to the point where we seldom heard it referred to as gout.

Dr. STETTEN. It might be mentioned, sir, if I might interject a remark, that the fact that the disease is rare need not militate against its study, because often from the study of rare conditions information of great value is obtained.

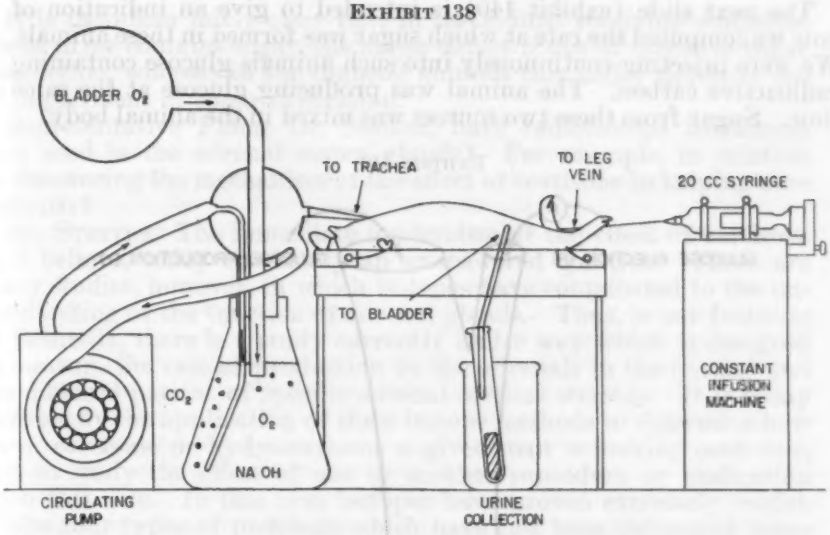
Representative PRICE. My questions were not directed to that. It was merely to establish if it was still prevalent, and perhaps we considered it in a different name or different form.

Dr. STETTEN. No; the disease is still recognized, and we have a number of patients from the Washington area that we are studying now in Bethesda.

The next slide (exhibit 138) represents the procedure we have applied in an attempt to measure the rates independently of glucose production and glucose utilization in the animal. The animal here is a rat.

The rat is receiving intravenously at a constant rate the solution containing glucose labeled with carbon 14. The expired air is continuously circulated in a fashion to permit the collection of the carbon dioxide which the animal exhales. From such experiments it is possible to calculate that quantity of glucose which is burned per unit of time.

EXHIBIT 138



The next slide (exhibit 139) shows such figures. Here are tabulated the quantities of carbon dioxide derived from body sugar. In control animals this answer came out to be approximately unity. Animals given alloxan develop a disease which is remarkably similar in certain regards to human diabetes. In such animals it was repeatedly observed that the quantity of sugar burned to carbon dioxide fell by a factor of two-thirds. This could be reversed to some degree by the administration of insulin.

EXHIBIT 139

Expired CO_2 Derived from Body Glucose

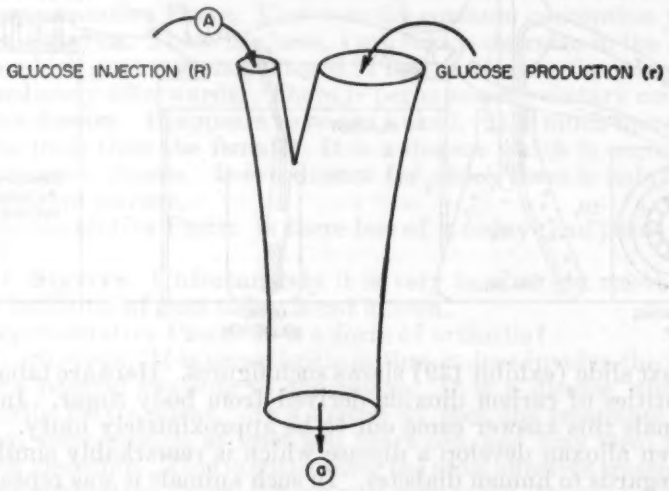
	per cent	mM/rat/hour
Control (333)*	21.3	0.97
Alloxan (83.3)	9.4	0.31
Alloxan (insulin) (83.3)	13.1	0.66
Cortisone (83.3)	26.8	1.25
Cortisone (167)	27.7	1.45
Cortisone (333)	16.7	0.95

*Figures in parentheses are rates of glucose injection in mg. per hour.

There is another situation in which animals and humans on occasion develop a disease which simulates diabetes. This is the consequence of overadministration or overproduction of adrenal cortical hormones. Here we found that the situation was quite different. There was no apparent impairment in these animals in the rate at which sugar was burned. On the contrary, they seemed to be burning sugar at normal or slightly better than normal rate.

The next slide (exhibit 140) is intended to give an indication of how we computed the rate at which sugar was formed in these animals. We were injecting continuously into such animals glucose containing radioactive carbon. The animal was producing glucose at the same time. Sugar from these two sources was mixed in the animal body.

EXHIBIT 140



We studied a sample of this mixture. Knowing the radioactivity in glucose injected, and the rate of injection, we measured the radioactivity of the glucose in the body and could calculate what fraction of this must be arising continuously from the animal's own tissues.

The last slide (exhibit 141) shows the results of such study. The rate of glucose production (r) in the diabetic rats was somewhat increased over control levels, but in the ones receiving cortisone it was increased by a factor of about eightfold.

EXHIBIT 141

Rates of Glucose Production

	Number of rats	R* mg/rat/hr	a† per cent	r** mg/rat/hr
Control	6	333.	95.0 ± 1.0	17.5 ± 3.8
Alloxan	6	83.3	65.8 ± 1.0	43.3 ± 1.8
Alloxan (insulin)	3	83.3	52.0 ± 1.5	76.9 ± 4.7
Cortisone	9	83.3	42.5 ± 0.7	112.7 ± 3.2
Cortisone	6	167.	57.4 ± 2.0	123.6 ± 5.1
Cortisone	6	333.	71.5 ± 1.4	132.7 ± 8.9

*Rate of glucose injection.
†(Activity of urinary glucose/activity of injected glucose) x 100.
**Rate of glucose formation.

It is therefore fairly clear that in the animal receiving cortisone, whose urine contains sugar, the major defect is one of excessive sugar production, whereas in the diabetic animals this major defect is one of impairment of sugar utilization.

Representative PRICE. Dr. Stetten, have radioisotope techniques been used in the adrenal cortex glands? For example, in relation to discovering the mechanism of the effect of cortisone in helping cure arthritis?

Dr. STETTEN. The immediate mechanism of the effect of cortisone is, I believe, today essentially an unanswered question. There are many studies, however, in which isotopes have contributed to the understanding of the function of adrenal glands. Thus, in our Institute at Bethesda, there is a study currently under way which is designed to measure the rate of production by the adrenals in the normal and the diseased patient of specific adrenal cortical steroids. It is today possible by the application of these isotope methods to determine how much cortisone or hydrocortisone a given man is making each day, and to study the effect of one or another procedure or medication upon this rate. In this area isotopes have proven extremely useful.

The four types of problems which have just been delineated cover fairly well the areas in which isotopic tracers have proven most useful in the past. This should not be taken to mean that other areas will not open up in the future. Already there is a suggestion that whereas hitherto we have exploited the great chemical similarities between isotopic siblings, we may in the future be equally interested in the small but useful difference in behavior between such twins of elements. The isotopic tracer techniques have become an intrinsic part of the laboratory machinery of medical research. The biologist is only beginning to take advantage of these developments of the physicist and the engineer. To those of us who for nearly 20 years have been involved in the application of isotopes to biological problems, the contribution of these techniques has been gratifying and promises in the future to be even more rewarding. Thank you.

Representative PRICE. Thank you very much, Dr. Stetten. Unfortunately, we probably missed part of your statement, but we will read it carefully in the record.

I wonder if you could just tell me the nature of your experiment here and your relationship with the Atomic Energy Commission on the study of arthritis.

Dr. STETTEN. You mean the relationship of our Institute at Bethesda and the Atomic Energy Commission?

Representative PRICE. Yes.

Mr. STETTEN. The Institute for Arthritic and Metabolic Diseases has, as has each of the seven Institutes in Bethesda, clinical and basic science branches. The basic science branches are devoted to chemistry, physiology, physics, biology. The clinical branches are devoted chiefly to the study of patient material involving the diseases arthritis and the related rheumatoid diseases, endocrine disorders or metabolic disorders of one sort or another.

Representative PRICE. Is the use of a research reactor required for your studies?

Dr. STETTEN. For our studies within our Institute I would say at this time probably not, sir. We derive great benefit from the Atomic

Energy Commission with whom we have a contract similar to other institutions. We secure materials and on occasion services from them.

Representative PRICE. Do you receive the radioisotopes from Oak Ridge?

Dr. STETTEN. Yes, sir.

Representative PRICE. Which radioisotope do you use?

Dr. STETTEN. In most of these studies that I have mentioned, carbon 14. In some of the studies I mentioned, we use stable isotopes interchangeably with radioactive isotopes as dictated by the problem. Of nitrogen or oxygen we have no useful radioactive isotopes, but we do have stable isotopes.

Representative PRICE. How long have you been working with radioisotopes in the study of arthritis?

Dr. STETTEN. I became involved in gout studies in 1947.

Representative PRICE. Thank you, Dr. Stetten. The committee certainly appreciates the fine presentations made this morning by all the witnesses. They were very well done and certainly contributed a great deal to the material the committee is assembling on the subject to make available throughout the country.

Thank you very much, Dr. Albert, for presenting these witnesses.

Dr. ALBERT. Thank you.

Dr. SWEET. Sir, before the hearing closes I think there is very much due from us an expression of our tremendous gratitude in the first instance to the legislators in this country who have devoted such a tremendous amount of their time to familiarizing themselves with the work of scientists. It must be an extraordinarily difficult task for you gentlemen in the midst of all your other duties to devote such an enormous fraction of your time to this kind of work. From contact with scientists in other countries, I have come to realize how peculiarly fortunate we are in having men like you in our House and our Senate. I am sure I speak for all of us here when I say that we are exceedingly grateful to you, sir, for devoting all of this time to hearing our studies in this very sympathetic way.

Representative PRICE. Thank you very much, Dr. Sweet; it is very kind of you to say that. I would like to point out here that the preamble of the first Atomic Energy Act stated that it was the intent of the Congress and the Government of the United States to devote a great part of the atomic energy program—the main part—to the peaceful uses of the atom. We have always felt dedicated to that. We have recognized the obstacles in the way of doing so. But this committee and Congress and I feel that the Commission have never lost sight of the fact that our main objective and our most sincere hope has been that the atom could be used for the benefit of mankind, rather than the destruction of mankind. You gentlemen in the scientific world are certainly contributing toward that objective.

The committee is certainly honored to have you here as witnesses, and we want to commend you for the work that you are doing. Thank you very much.

The committee will be adjourned until tomorrow morning at 10 o'clock, and we will meet again in this same chamber.

(Thereupon, at 12:50 p. m., Wednesday, June 6, 1956, a recess was taken until Thursday, June 7, 1956, at 10 a. m.)

PROGRESS REPORT ON RESEARCH IN MEDICINE, BIOLOGY, AGRICULTURE, AND FOOD PRESERVATION

THURSDAY, JUNE 7, 1956

CONGRESS OF THE UNITED STATES,
SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT,
JOINT COMMITTEE ON ATOMIC ENERGY,
Washington, D. C.

The subcommittee of the Joint Committee met at 10 a. m., pursuant to adjournment, in the Old Supreme Court Chamber of the Capitol, Hon. Melvin Price (chairman of the subcommittee) presiding.

Present: Representatives Price (presiding), Cole, and Patterson; and Senator Bricker.

Representative PRICE. The subcommittee will be in order.

This is a continuation of a hearing of the Subcommittee on Research and Development to see the progress reports on the use of atomic energy in the field of medicine.

Dr. Dunham, would you proceed with the witnesses today?

Dr. DUNHAM. This morning, Mr. Chairman, the series of reports will begin with that by Dr. Herrman L. Blumgart, professor of medicine at the Harvard Medical School, and physician in chief of the Beth Israel Hospital. He will discuss the use of radioiosotopes in cardiovascular disease.

STATEMENT OF DR. HERRMAN L. BLUMGART, PROFESSOR OF MEDICINE OF THE HARVARD MEDICAL SCHOOL, BOSTON, MASS.

Dr. BLUMGART. Mr. Chairman, and Dr. Dunham, the chief isotope that is used in the treatment of cardiovascular disease is radioactive iodine, I–131. The object of using this isotope is to eradicate all or part of the thyroid gland, to lessen the needs of the body for oxygen and thereby reduce the work of the heart. The rationale of the treatment is, in brief, that lowering the total metabolism of the body so reduces systemic circulatory requirements as to place them within the limit of cardiac reserve.

The association of the thyroid and heart disease has a long and honorable tradition. Indeed, the first description of hyperthyroidism was by Dr. Parry, one of the eminent physicians of the Bath School, who first described hyperthyroidism in 1786. Interestingly enough, this description of hyperthyroidism appears in his book under the heading "Disesases of the Heart." He noticed that when the thyroid increased in size, the patient had great difficulties in respect to his heart.

Representative PRICE. I am sorry to interrupt at this early time, but I see we have a quorum call in the House, and I think if I get over there early I can be back here in 10 minutes and then we can proceed, I think, most of the morning without further interruption.

We will suspend for just a moment.

(A short recess was had.)

Dr. BLUMGART. Mr. Chairman, as I was saying, we are thinking mainly of the heart here as a pump and the work it has to do, and seeing whether if we affect the thyroid gland by lowering the metabolic rate and therefore requiring the heart to do less work, whether the symptoms of heart disease, particularly pain in the heart such as angina pectoris or the failure of the pump as a whole, congestive heart falure, manifested by shortness of breath, swelling of the legs and dropsy are favorably affected.

This association between thyroid function and its effect on the heart was first noted clinically by Dr. Caleb Hillier Parry in 1786. He noticed that when the thyroid became larger and, as we now know, functionally hyperactive, the patients had more cardiac pain and also had the evidences of swelling of the legs and marked breathlessness. Likewise, he noticed that when the thyroid in the neck became smaller, these cardiac patients felt much better.

Throughout the 19th century, a great deal of interest was displayed, particularly by the surgeons who operated on people whose thyroid function was abnormally increased. They noted that with the reduction of cardiac work after extirpating part of the thyroid, the cardiac patients were better.

Now, with the advent of radioactive iodine, which has a marked avidity for the thyroid, many patients who have hyperactive thyroid glands may be treated with radioactive iodine and their metabolic rate returned to normal. In many of these people there may be a degree of heart disease which causes the heart to fail when it has to do the inordinate amount of work imposed by a hyperactive thyroid gland. But once the heart is relieved by this inordinate demand it may be competent to meet the lesser needs of the body. The patient may then feel well as he "lives within the income of his circulation."

Since 1947, a group of us, including Dr. A. Stone Freedberg, Dr. George S. Kurland, and Dr. Robert Buka and others, have addressed ourselves to the question whether patients with the cardiac pain of angina pectoris whose thyroid was functioning normally, might experience benefit if we gave radioactive iodine, destroyed the normal thyroid gland and thereby reduced the amount of cardiac work.

We have now been working in this field for some 9 years. Our work may be summarized for the purposes of this discussion as follows: We have taken only a small group of patients who, despite all the known methods of treatment for heart disease, still are miserably afflicted. For most people, the vast majority of people who have dropsy (congestive failure) or those with angina pectoris, the well-established methods of treatment provide a satisfactory and comfortable regime of life. But there is this small group of people, probably not more than 5 percent of the total population of people who have angina pectoris or congestive heart failure who, despite all treatment, are miserable. They have repeated pains during the day. They are unable to sleep during the night. They cannot work. They are really too sick to be able to enjoy life, and they are not sick enough to die. They may remain in this State for many years. For this

small group of people who are chronically afflicted, many procedures have been proposed. Practically all of these procedures are surgical procedures, such as putting foreign substances in the pericardium, or anastomosing vessels to the heart in the hope that these new vessels from outside the heart may supply enough blood. The method which we are discussing this morning, is a medical measure which consists of giving radioactive iodine to depress the normal thyroid function, and carries with it no risk, pain, or invalidism.

We have treated a small group consisting of approximately 150 patients. We felt additional evidence of the theropeutic value of this method would be afforded by survey throughout the country of those clinics who had adopted this method of treatment and had had several years of experience. Therefore with the help of the Atomic Energy Commission, we sent a questionnaire to all clinics using radioactive iodine to learn the number of patients they had treated by this method and the results they had obtained. In this questionnaire we characterized the degree of improvement as excellent or good or not worthwhile.

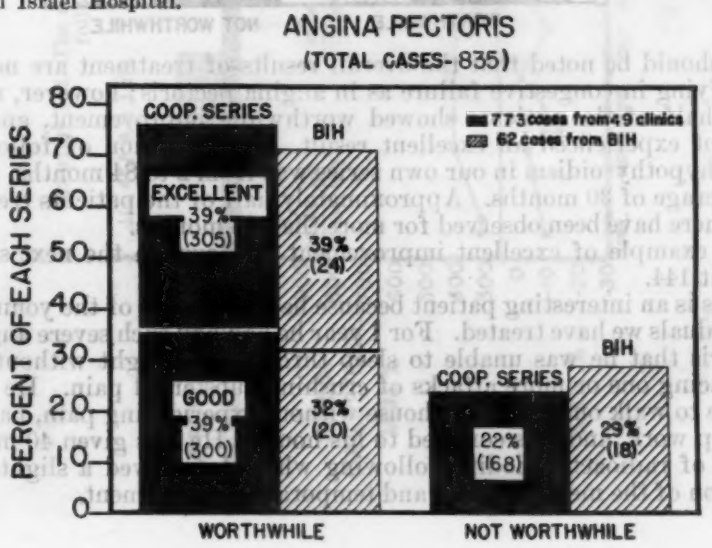
An excellent result denotes that the patient is markedly improved over pretreatment status, with either no recurrence of symptoms or a marked decrease in the frequency and severity of angina pectoris or congestive failure, despite markedly increased activity; in many instances rehabilitation and return to gainful employment occurred.

A good or worthwhile result denotes definite improvement, with a decrease in frequency and severity of attacks of angina pectoris or congestive failure on the same amount of activity as before treatment. In the remainder of the patients, there was no worthwhile improvement.

ANGINA PECTORIS

The results in the 835 patients with angina pectoris, approximately 200 of whom also had evidences of congestive heart failure, are shown in exhibit 142: 78 percent of the patients treated elsewhere showed

EXHIBIT 142. Results of radioactive iodine treatment of 835 euthyroid patients with angina pectoris in a cooperative series and in a group of cases studied at Beth Israel Hospital.



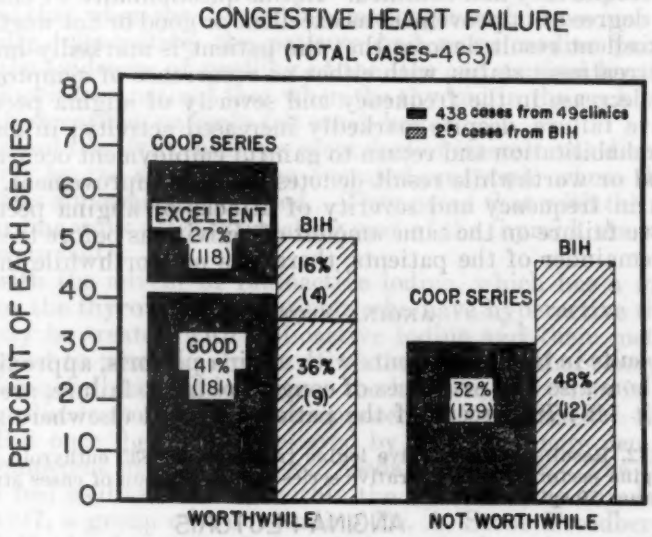
worthwhile improvement; 39 percent showed excellent results, and 39 percent showed good results; 22 percent showed no worthwhile result.

Our own experience, shown in the right hand columns of figure 1, was quite similar.

CONGESTIVE FAILURE

The results in the treatment of 463 patients with congestive failure are shown in exhibit 143: 68 percent of the patients treated elsewhere showed worthwhile improvement; 27 percent showed excellent results, and 41 percent showed good results. The remainder 32 percent failed to show improvement. Our own experience, denoted in the right-hand columns of exhibit 143, is quite similar.

EXHIBIT 143. Results of radioactive iodine treatment of 463 euthyroid patients with congestive failure in a cooperative series and in a group of cases studied at Beth Israel Hospital.



It should be noted that the overall results of treatment are not as gratifying in congestive failure as in angina pectoris; however, more than half of the patients showed worthwhile improvement, and 27 percent experienced an excellent result. The duration of followup after hypothyroidism in our own series was from 2 to 84 months, with an average of 30 months. Approximately half of the patients treated elsewhere have been observed for more than 18 months.

An example of excellent improvement is shown in the next slide, exhibit 144.

This is an interesting patient because he was 41, one of the youngest individuals we have treated. For 1 year he had had such severe angina pectoris that he was unable to sleep through any night without experiencing one or more attacks of crushing substernal pain. He was unable to walk outside of his house without experiencing pain, had to give up work, and was confined to his house. He was given 40 millicuries of radioactive iodine following which he showed a slight depression of the metabolic rate and temporary improvement.

EXHIBIT 144. The serum cholesterol, basal metabolic rate, and the clinical course following 5 doses of I-131 totaling 150 millicuries.

After additional doses we produced a marked depression of his thyroid function, and he showed marked improvement. The beginning of the improvement was in August 1948. He was able to walk and then finally to work. He has been working at least 8 hours a day ever since up to the present time in 1956. To the present he has had almost 8 years of gainful employment. During the first 3 years he had no pain whatsoever while working, and in the last 3 years he has slight substernal tension on walking rapidly upstairs, particularly in cold Boston weather.

The next slide shows a patient who had had angina pectoris for 10 years (exhibit 145). She had had three prior coronary attacks, and was completely invalided at home. She had severe attacks at night as well as during the day requiring demerol injections at least 3 or 4 times a week.

You see again that on treatment, after 10 years of invalidism, her improvement was marked and she was able to go out shopping, to accompany her husband on social engagements and really enjoy life for a period of approximately 3 years, to the age of 70. Then, unfortunately, she experienced a fourth coronary attack, and died. She had had 3 years of worthwhile existence, however.

This case is again illustrative of a worthwhile result.

CRITERIA FOR SELECTION OF PATIENTS

Patients with angina pectoris who may be expected to gain the greatest benefits from treatment with I–131 are those in whom the disease, regardless of its severity, has been relatively stationary or only slightly progressive over a period of 1 year or more. Patients with congestive failure should show evidence of some cardiac reserve, such as improvement in signs of congestive heart failure and other symptoms on bed rest or with the use of diuretics and digitalis. A basal metabolic rate of more than −10 percent is desirable. It is important that the patient be alert, cooperative, and emotionally stable. It has been our experience that hyperactive, tense patients are particularly favorable candidates.

The very recent onset of angina pectoris or of status anginosus, or other evidence of rapidly progressive cardiovascular disease, is considered by us a contraindication to I–131 therapy. In this connection it should be emphasized that we have no reason to believe that hypothyroidism retards the progression of the underlying pathological process. The treatment of heart disease with I–131 is not to be considered as curative; it is a palliative procedure that is to be regarded as an adjunct to recognized medical measures. It is unwise to treat patients who are in terminal phases of their disease, particularly since 2 to 6 months intervene before the hypometabolic state is attained. Some clinics, in contrast to our own earlier experience, have not regarded rapidly increasing angina pectoris or congestive failure, intermittent claudication, or low metabolic rate as contraindications to treatment; further detailed studies are required to settle these points.

Several clinics reported the use of single doses of I–131 as high as 50 millicuries. Reports from those clinics indicate, as might be anticipated on the basis of earlier experience, that some of their patients suffered temporary aggravation of their angina pectoris or congestive

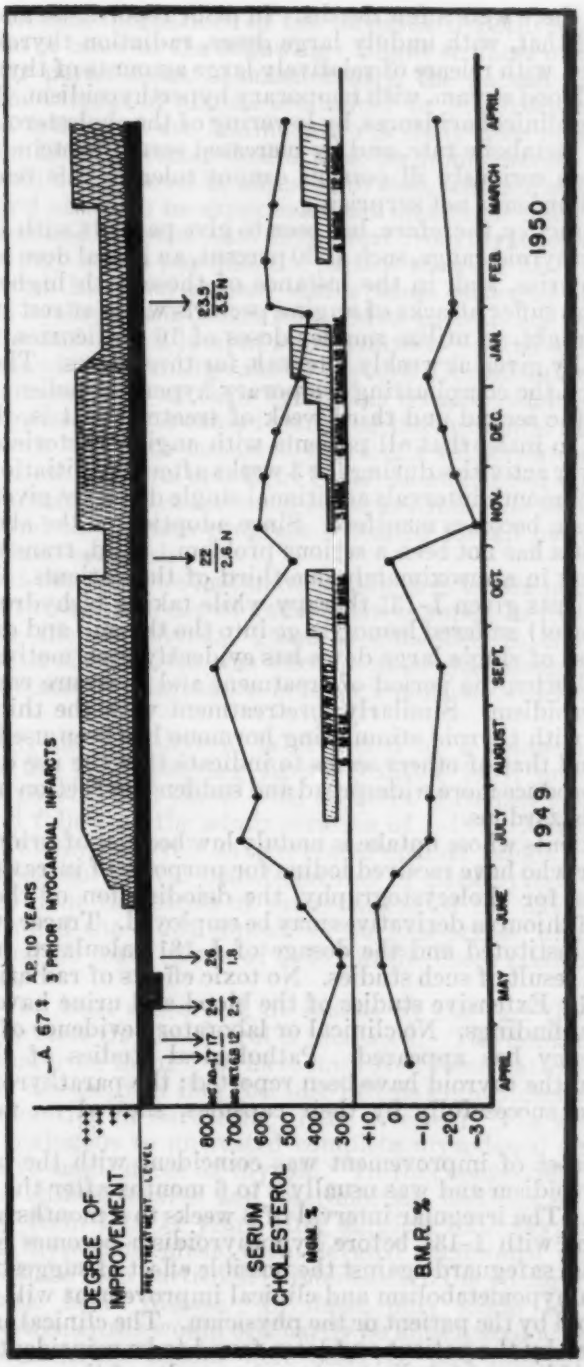


EXHIBIT 145. The serum cholesterol, basal metabolic rate, and the clinical course following administration of I-131.

failure; there were a few deaths. In prior reports, we and others have observed that, with unduly large doses, radiation thyroiditis may be associated with release of relatively large amounts of thyroid hormone into the blood stream, with temporary hyperthyroidism. This is manifested by clinical evidences, by lowering of the cholesterol level, by rise in basal metabolic rate, and by increased serum protein bound iodine. That such seriously ill persons cannot tolerate this temporarily increased burden is not surprising.

Our practice, therefore, has been to give patients with I–131 uptakes in the euthyroid range, such as 30 percent, an initial dose no larger than 20 millicuries, and, in the instance of those with higher uptakes or those who suffer attacks of angina pectoris while at rest in bed or during the night, to utilize smaller doses of 10 millicuries. These doses are usually given at weekly intervals for three doses. The period during which the complicating temporary hypermetabolism may occur is usually the second and third week of treatment; it is, therefore, our practice to insist that all patients with angina pectoris decubitus restrict their activities during the 3 weeks after the initiation of therapy. At 1- to 2-month intervals additional single doses are given until hypothyroidism becomes manifest. Since adoption of the above program, thyroiditis has not been a serious problem. Mild, transitory thyroiditis occurs in approximately one-third of the patients. In 1 clinic, 1 of 3 patients given I–131 therapy while taking bishydroxycourmarin (Dicumarol) suffered hemorrhage into the thyroid and died.

The use of single large doses has evidently been motivated by a desire to shorten the period of treatment and to secure earlier onset of hypothyroidism. Similarly, pretreatment with the thiourea derivatives or with thyroid stimulating hormone has been used. Our experience and that of others seems to indicate that the use of these measures to produce more widespread and sudden destruction of the thyroid may be hazardous.

In patients whose uptake is unduly low because of prior ingestion of iodine or who have received iodine for purposes of intravenous pyelography or for cholecystography, the deiodination of the thyroid by means of thiourea derivatives may be employed. Tracer studies should then be instituted and the dosage of I–131 calculated in accordance with the result of such studies. No toxic effects of radiation have been observed. Extensive studies of the blood and urine have revealed no abnormal findings. No clinical or laboratory evidence of parathyroid insufficiency has appeared. Pathological studies of the radiation effects on the thyroid have been reported; the parathyroids evidently protected successfully by their capsules, showed no morphological changes.

The onset of improvement was coincident with the occurrence of hypothyroidism and was usually 2 to 6 months after the initiation of therapy. The irregular interval of 8 weeks to 6 months after the first treatment with I–131 before hypothyroidism becomes evident is an additional safeguard against the possible effect of suggestion; the time at which hypometabolism and clinical improvement will occur cannot be foretold by the patient or the physician. The clinical improvement, first noted by the patient and later found to be coincident with the inception of hypometabolism, when the results of the serum cholesterol and basal metabolic determinations are made available, is consequently the more impressive.

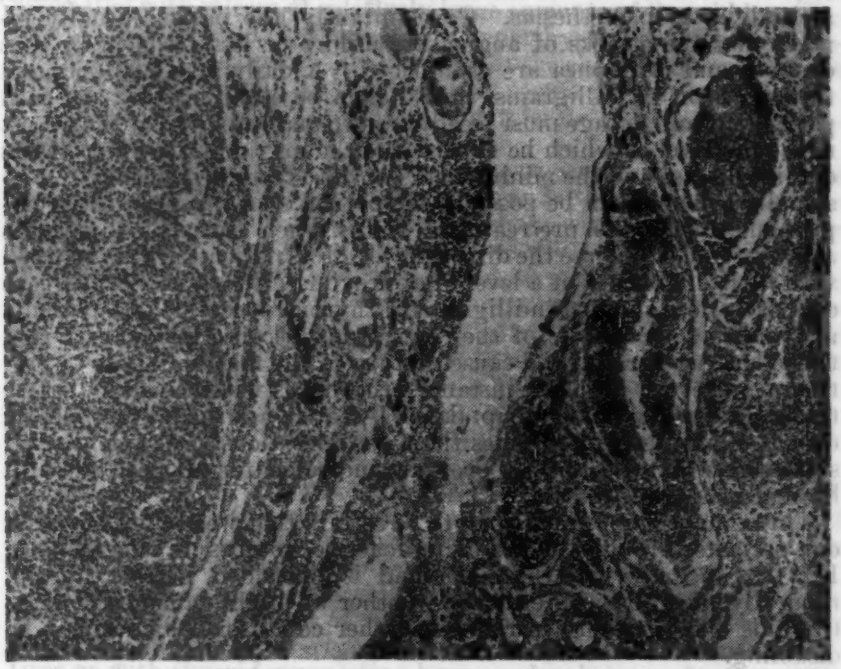
The first clinical intimations of the incipient hypothyroidism may consist of one or more of the following: Slight stiffness of the joints, arthralgia, or paresthesias. Concomitantly, the patient usually reports that the attacks of angina are milder or less frequent or that dyspnea and orthopnea are diminished. A daily dose of desiccated thyroid, 6 or 12 milligrams, should then be administered. In each patient thyroid dosage must be adjusted to maintain him at the lowest metabolic level at which he experiences the maximum relief from his cardiac disease and the minimum discomfort from myxedema. Occasionally this may not be possible, the patient showing little or no improvement over his pretreatment status when sufficient thyroid is administered to obviate the discomfort. Most patients are maintained with little discomfort at a level of approximately −20 to −25 percent on a daily dose of 6 to 30 milligrams of thyroid. Occasionally, patients may suffer a recurrence of their symptoms because residual thyroid tissue has regenerated and caused return of the metabolic rate to pretreatment levels. In such instances, thyroid is withdrawn and, after tracer doses show adequate uptake of I–131, an additional therapeutic dose is administered. Besides these considerations, the same careful supervision and therapeutic program indicated for all patients with heart disease are essential.

Throughout our work we had to be certain that we are not harming our patients through the use of radioactive isotopes, in this instance I–131. Since the parathyroid gland is imbedded in the thyroid, naturally one of our concerns was whether we might damage the parathyroids and therefore introduce another condition which might be disabling.

Fortunately, the parathyroid is protected by a connective tissue capsule. In the accompanying figure (exhibit 146), one observes here normal parathyroid tissue with adjacent shrunken and scarred thyroid gland following the administration of I–131. Measurements of the serum Ca and P levels have revealed normal values. Likewise there have been no clinical manifestations of parathyroid disorder. We have also done thousands of examinations of the blood and the urine and studied the I–131 content of various organs of the body. We have found no toxic effects of I–131 in the doses needed to treat these patients.

We have also been concerned, of course, by the fact that in this hypometabolic state the cholesterol is increased. The question, therefore, arises that even though we have improved these patients insofar as their heart disease, will they, because of this high cholesterol level, show an acceleration of hardening of the arteries? The situation is not strictly analogous to untreated complete myxedema, since these patients receive small doses of thyroid. In this connection, we have reviewed the clinical course and post-mortem findings of patients who survived from 1 to 11 years after surgical total thyroidectomy and in whom hypometabolism with elevated cholesterol values was present. We have been particularly interested in the younger patients with rheumatic heart disease. In them, only slight or minimal coronary arteriosclerosis would ordinarily be anticipated at death. If decided arteriosclerotic lesions were observed post mortem in such patients, the lesions might well be attributed to the myxedematous state. In a study reported elsewhere, the clinical and post-mortem

EXHIBIT 146. A normal parathyroid adherent to a thyroid gland showing marked fibrosis following administration of I–131 (X100).



findings are reported of 8 such patients with rheumatic heart disease or cor pulmonale, in which hypothyroidism or myxedema was present and who survived from 1 to 13 years (average, 7.4 years) following surgical total thyroidectomy. None of the 8 cases showed complete occlusion of any of the coronary arteries, 5 of the 8 showed no narrowing of any of the main stems or branches of the coronary arteries; only 3 of the 8 showed slight narrowing of one of the main stems. In the other arteries elsewhere in the body, damage from atheromatosis and atherosclerosis varied greatly, but conditions were similar to those usually observed in similar euthyroid patients.

Our results do not of course disprove a role of cholesterol in the production of atherosclerosis. These results do demonstrate, however, that over the observed period of time the hypothyroid state, controlled with small daily doses of desiccated thyroid, is not necessarily in itself sufficient cause for the production of coronary atherosclerosis.

The question naturally arises whether I–131 treatment of heart disease prolongs the duration of life. Statistical analysis of our data does not yield a decisive answer to this question. It appears that duration of life of these severely ill patients had not been decreased and may have been prolonged; future studies may well clarify this point.

In brief, to summarize this aspect of our studies, we may say that we have found that hypothyroidism may be induced in every cardiac patient that we have treated. In the patients with angina pectoris, approximately 75 percent secured a worthwhile result, half of them an excellent result, and half a good result. Well over 50 percent of

the patients who had congestive failure were improved. In addition to results which I have shown you here this morning, there are other favorable reports from foreign countries. In the clinical management of these patients, small daily doses of thyroid are usually administered to maintain the lowest metabolic rate consistent with comfort.

Another aspect studied particularly by Dr. Freedberg to which I shall devote only a few minutes, if I may, Mr. Chairman, is the medical effects of isotopic radiations on various tissues. In I–131 we have an isotope with radiant energy and in treating cardiac patients with normal thyroid glands we are dealing with normal tissue. We are able, therefore, to gain knowledge regarding the effect of radiation on normal human issue. Through the support of the AEC we are carrying on these studies for some years. In no patient treated to date have we observed any evidence of carcinogenesis, either clinically or by examining the thyroid area after death.

In studies on approximately 40 patients, significant functional changes occurred in the uptake and turnover of iodine by the thyroid approximately 7 days following administration of 5 to 30 millicuries and before the occurrence of discernible histologic changes. These radiation functional changes may be reverted to normal by the administration of the thyroid stimulating hormone of the pituitary. The sequence of structural changes in the thyroid occurring after 7 days have been studied over the ensuing months and years in different patients.

In the dosage range of up to approximately 1 millicurie delivering approximately 2,500 R. E. P., no change in thyroid gland I–131 uptake or turnover was observed on the administration of a second dose. On the other hand, doses of 2.1 to 3.0 millicuries delivering 5,000 to 6,000 R. E. P., respectively, were followed by depression of thyroid gland I–131 uptake and an increased turnover of the second dose.

Representative PRICE. Thank you very much, Doctor.

Are there any questions?

Senator BRICKER. Is it necessary in practically all of these treatments to completely destroy the function of the thyroid or can you do it in a graduated way and control the output of thyroxine?

Dr. BLUMGART. That is a very interesting question, sir. There are a few patients who, after several doses of I–131 are at a desirable intermediate hypometabolic level. They do not have to take thyroid by mouth. Unfortunately, most of those individuals eventually show an increased thyroid function, and a return of their angina pectoris. We then have to treat them again. Therefore, practically all of our patients at this time would be myxedematous without medication and therefore are taking to 30 milligrams of thyroid daily.

Senator BRICKER. You feel that you can control the body metabolism better by the medication than you can control the output of the thyroid?

Dr. BLUMGART. Exactly, we can govern the metabolic and clinical level.

Representative PATTERSON. Doctor, do you connect any of these heart cases with thyroid and cholesterol functions?

Dr. BLUMGART. That is to say there are two types. There is one in whom the thyroid is hyperfunctioning, and therefore, the demands on the heart are inordinately increased. In the other group are the vast majority of cases with angina pectoris in whom the thyroid is normal. It is normal by all of the measurements. They are clinically normal

in respect to their thyroid function, their metabolism is normal and the uptake of tracer doses of iodine I–131 is normal.

When we depress the thyroid function, the cholesterol level rises but is reduced or abolished by the administration of small doses of thyroid.

Senator BRICKER. There is a relationship then, between the cholesterol content and the metabolism?

Dr. BLUMGART. When we depress the metabolism, the cholesterol value generally rises.

Representative PRICE. You have made a very interesting presentation.

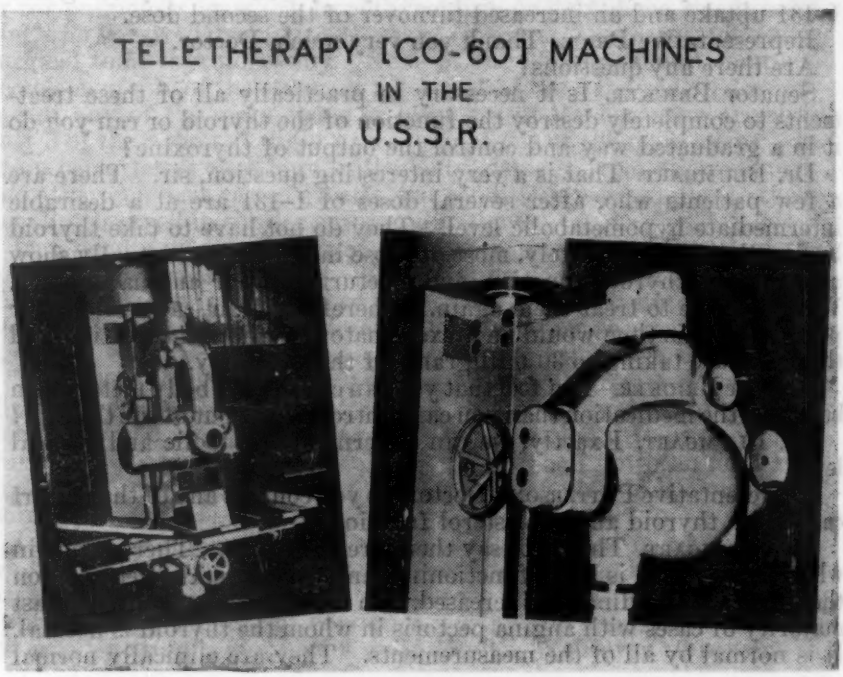
Dr. DUNHAM. Mr. Chairman, the next speaker is going to be Dr. Marshall H. Brucer, chairman of the Medical Division of the Oak Ridge Institute of Nuclear Studies. He reported to you 2 years ago in a general statement of the activities of that group. Today he is going to confine his remarks largely to bring you up to date on the status of radioisotope teletherapy.

STATEMENT OF DR. MARSHALL H. BRUCER, MEDICAL DIVISION, OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, OAK RIDGE, TENN.

Dr. BRUCER. Two years ago teletherapy was a relatively new thing, but it has caught on very rapidly all over the world. I would like to show you what has happened in the teletherapy field throughout the world.

On exhibit 147 are pictures of two of the Russian machines that were shown at Geneva last summer. There were very well made machines,

EXHIBIT 147



although they are using levels of activity that are somewhat lower than we are using, it is a very useful level, and we are also building some machines at about the same level of activity. The Russian machines use about 20 and 250 curies of cobalt 60.

Exhibit 148 shows a couple of machines that were built and have been put into operation in Holland, and in Sweden, The machine from Holland uses about a kilocurie or two of activity. The Swedish machine is just now beginning to be sold in this country; it is devised for a very small amount of cobalt 60, 10 curies of activity, rather than the kilocurie amounts.

EXHIBIT 148

On exhibit 149 we show what has happened in England. England has produced many of these teletherapy machines. The first example is a kilocurie machine that will take thousands of curies of cobalt, the second uses a few hundred curies of cobalt.

EXHIBIT 149

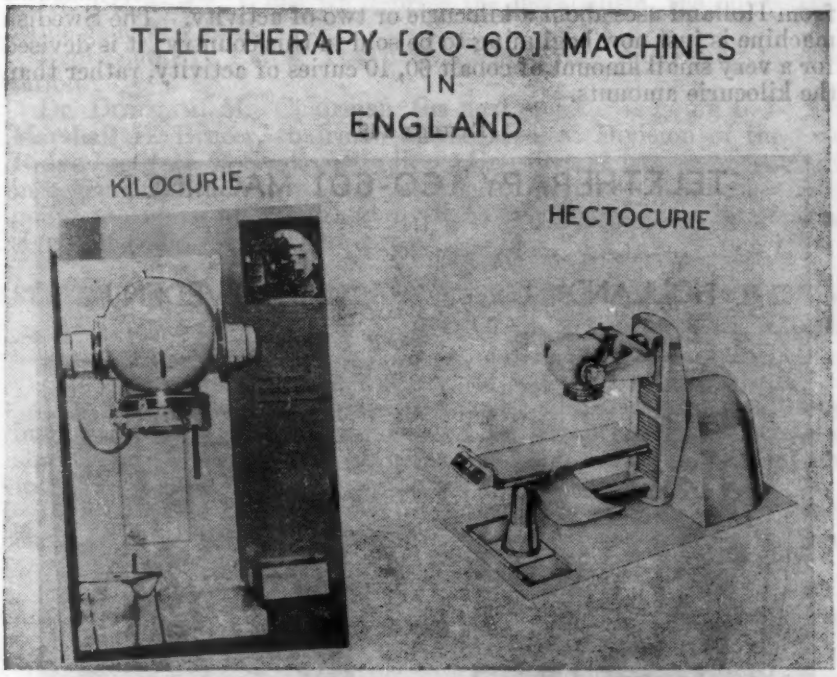


Exhibit 150 shows pictures of two other examples of the English machines. These were the first two machines that were devised in England. Both are at the Bristol Hospital. The smaller machine was originally designed for 20 curies of activity because of the problems of source production; but when they finally got the source, it turned out to be 200 curies, and so this is now a 200-curie machine. The other machines were designed for 400 curies of activity.

Japan has had a hard time getting activity for their machines, but they have devised machines that are much more like the American machines. The Japanese physicists have devised two kinds of machines. The large machine shown on exhibit 151 is devised for 2,000 curies of activity, and it is now in operation with 100 curies of activity.

EXHIBIT 150

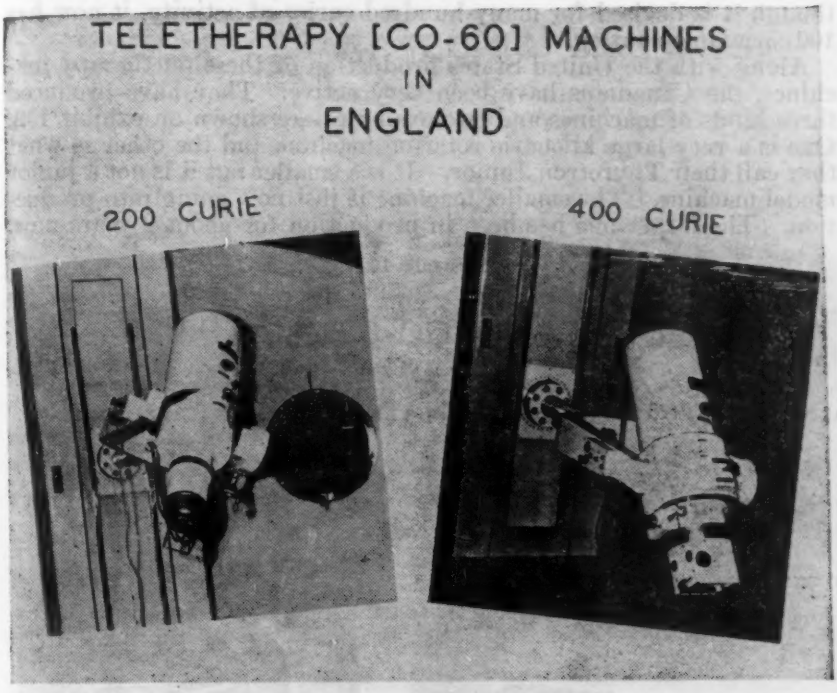


EXHIBIT 151

The smaller rotational machine has recently been activated. Although it is devised for many hundred curies of activity, it now has 100 curies in operation.

Along with the United States production of these teletherapy machines, the Canadians have been very active. They have produced three kinds of machines and two examples are shown on exhibit 152. One is a very large kilocurie rotating machine and the other is what they call their Thyrotron Junior. It is a smaller but it is not a junior model machine. The smaller machine is just now going into production. The larger one has been in production for about 2 years now.

EXHIBIT 152

The next few exhibits show some of the United States machines. Exhibit 153 (left) is a kilocurie machine that was devised by the Picker Co., and it is made for a few thousand curies of activity. Since this kilocurie machine is a relatively expensive device, the hectocurie machines (exhibit 153, right) were devised about 2 years ago for the purpose of using smaller amounts of activity and to save on the capital investment. The Barnes-Keleket hectocurie machine now is a very popular machine throughout the world.

Exhibit 154 shows many other United States devices. These are not the only ones that have been made. Many others have been devised in this country. One is a very small hectocurie machine built at Georgia Tech University and installed at the Emory University Medical School. Another is the Bar-Ray machine, which was devised by the Brookhaven National Laboratory for the New York Operations Office of the Atomic Energy Commission for the irradiation of small animals and for radiobiological studies. It was built and then adapted by the Bar-Ray Co. for human therapy.

EXHIBIT 153

EXHIBIT 154

The same exhibit shows the General Electric machine that was devised many years ago. It is actually the first cobalt machine to be built and put in operation. Next is the City of Hope machine, which was devised and built by them to fit their own special needs. Another is an early Picker rotational machine, which, you can see, was designed to perform the same type of rotation as the Canadian machine. The last picture on this exhibit shows one of the hectocurie machines adapted by the Cedars of Lebanon Hospital, with a closed circuit television set and a small dental X-ray machine attached to it, to make a very complex but easily controlled experimental rotational machine.

Let us look at exhibit 155, where we can summarize what has happened in the last few years in the growth of the teletherapy program.

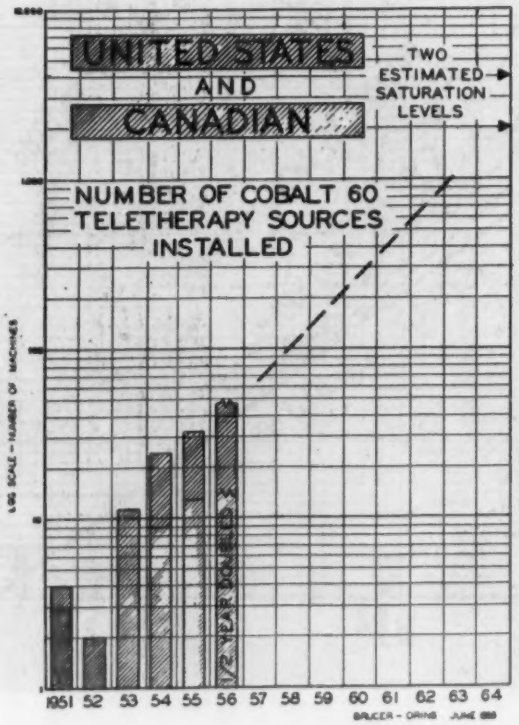
Cobalt 60 teletherapy sources are being produced now by the Canadian reactors and by the United States reactors (exhibit 155, left). The production started in 1950, with the United States producing a small source. We find that there has been a steady increase in production up to 1956. (I have doubled the 1956 amount to put it on scale with the other years.) The United States sources are shown in blue on this chart, and the Canadian sources in red. The reason for the decrease in Canadian sources during 1 or 2 of these years is that the Canadians have taken the brunt of the experimental production program and have had some difficulties with their reactor in the production of sources.

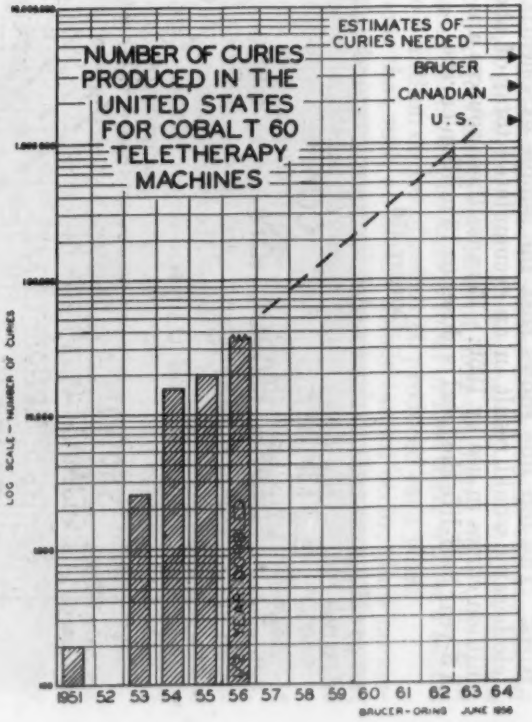
In getting accurate figures and trying to make an estimation of what is going to happen in the teletherapy field for the production of sources in the future, we have used the figures for the number of curies of cobalt 60 for the United States and not the number of sources (exhibit 155, right). For a prediction of the future I have projected the growth, and I will show the reasons for this projection later. Many of us in this country and in Canada have tried to make some sort of an estimate of what is going to be needed during the next 5 to 10 years. It takes about 2 years to manufacture a teletherapy source; that is, from the raw cobalt to a hot radioactive cobalt 60 source in operation. Therefore, these predictions have to be made in order to meet the growing demand for the sources. The prediction that I have made is that 10 years from now, by 1966, there would be an accumulated total of about 4 million curies of cobalt used just for teletherapy alone throughout the world. A Canadian prediction is about 2½ million curies, and one of the other United States predictions is 1½ to 2 million curies for this country alone, and not for the world.

EXHIBIT 155

THE GROWTH OF TELETHERAPY

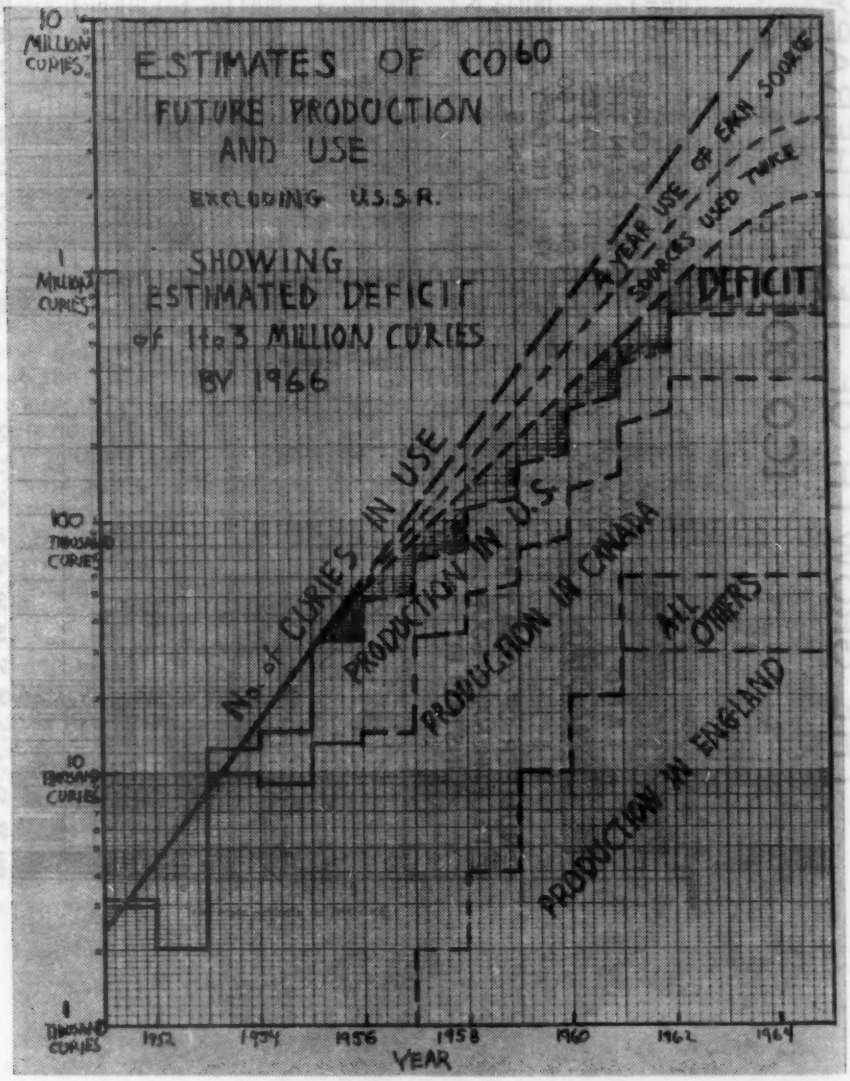
[CO 60]





On exhibit 156 I have broken down the estimate into its component parts. The top line shows that the simple exponential growth of teletherapy would result in an accumulated total of about 30 to 50 million curies in use by 1956. Because these sources are decaying on a 5-year half-life the total is closer to 13 million curies.

EXHIBIT 156



However, each source is used for about 3 to 4 years in any one machine and therefore the total accumulated number of curies in use in any one year will be closer to about 4 million curies. Since some of these sources will be used twice, a better estimate is probably about 2 million curies.

The lower part of the graph shows the production in yearly steps of cobalt 60. The production estimates are based on the announced plans for cobalt 60 production. It is apparent since the graph uses a logarithmic scale, that on the basis of these estimates there will be an ever-increasing deficit of production until in 1966 there will be a deficit of from 1 to 3 million curies of cobalt 60 produced each year.

It is obvious that such an actual deficit cannot occur, since no machine can go into operation until it has a cobalt 60 source. However, there will be a real deficit in terms of the producers not meeting the demands of the consumers.

Let us look at exhibit 157 and see the basis for my predictions of what the production of cobalt 60 will have to be. This is a very difficult kind of thing to predict because it depends upon what the radiotherapists throughout the world think of these sources after they have used them for a certain length of time. What I have done in making this kind of prediction (exhibit 157, left) is to take the number of deep therapy X-ray machines now in existence; there are in Europe, for example, something like 2,000 deep therapy X-ray machines now operating. Most of these are 200 to 250 kilovolt X-ray machines. In the United States there are almost exactly 1,850. This is the only reliable figure in all of my estimates.

EXHIBIT 157

BASIS FOR PREDICTION OF

THE WORLD NEED FOR

TELETHERAPY [CO 60, CS 137] SOURCES

EXCLUDING U.S.S.R.

ESTIMATED NUMBER OF DEEP THERAPY X-RAY MACHINES

EUROPE	2000
UNITED STATES	1800
JAPAN AND EAST	1000
SOUTH AMERICA	600
ENGLAND	500
AFRICA	350
CANADA	200
AUSTRALIA, NEW ZEALAND	100
TOTAL	6550

ASSUME—

SOME WILL NEVER BE REPLACED WITH CO 60

SOME CO 60 SOURCES WILL BE USED TWICE

1000 CURIES (CO 60 EQUIVALENT) AVERAGE PER MACHINE

ESTIMATED NUMBER OF CO 60 CURIES NEEDED BY 1961
3 TO 5 MILLION CURIES

1956 PLANNED GOALS FOR PRODUCTION BY 1961 MILLIONS OF CURIES

UNITED STATES	0.5
UNITED STATES (CS-137)	0.05
CANADA	1.0
ENGLAND	0.5
JAPAN	0
SWEDEN	0
NORWAY	SMALL
ITALY	0
INDIA	0
SOUTH AMERICA	0
FRANCE	?

TOTAL — 2.05 MILLION CURIES

DEFICIT

1 TO 3 MILLION CURIES

In Japan, and the rest of the East, we think there are about 1,000 machines. In South America there are 600; and 500 in England; in Africa, 350; and in Canada, about 200; and Australia and New Zealand, about 100.

Representative PRICE. How do you account for a larger number of these machines in Africa, where we do not know of any known atomic energy program, than in Canada?

Dr. BRUCER. These figures are for electrically generated X-ray machines and are based upon modified population densities. Since the cobalt machines are taking the place of the 200-kilovolt electrically generated machines, this is our best way of making an estimate of how much cobalt will be needed.

Representative PATTERSON. How are these employed now?

Dr. BRUCER. The patient goes to see his doctor, and the doctor decides that the patient needs deep X-ray therapy. About three-quarters of the X-ray therapy is used for the treatment of tumors.

Representative PATTERSON. Regardless of whether it be benign or malignant?

Dr. BRUCER. Usually malignant. The tumor is diagnosed as malignant first and then the decision might be that X-ray therapy should be used. Throughout the world now, the most common kind of X-ray therapy is with the 200-kilovolt so-called deep therapy X-ray machine. These are the machines that are being replaced in this country with cobalt machines.

Representative PRICE. It is still interesting that you have more X-ray machines in Africa than in Canada.

Dr. BRUCER. The figures are based upon population. The only estimates we have on the number of X-ray machines indicate that only in the northern part of Africa and in the very south of Africa are there many of these X-ray machines in operation.

Representative PRICE. The Union of South Africa, and then all through north Africa, Morocco.

Dr. BRUCER. Our figures are primarily from Egypt, and the Union of South Africa. Now, for the rest of Africa, we have no figures. These estimates may be very wrong but they are the best we can get. Apparently something like a little over 6,000 deep therapy machines are in operation, outside of the Soviet Union, where we have no figures.

If this is true, then we will make a certain number of assumptions on what is going to be needed for cobalt machines in the future. We make the assumption that some of these X-ray machines will never be replaced with cobalt-60 machines. We are also making the assumption that most of them will be. At the present time, many therapists would like to replace their 200-klovolt X-ray electrically generated machines with cobalt 60, if cobalt 60 were available. In addition we may assume that the hospital population will double, that there will be other competing uses for cobalt and other factors that make my predicted figures very conservative.

Some of the cobalt-60 sources will be used twice, because some of these machines, as you have seen, are for 2,000 curies of activity, some are for 1,000 curies, some are for 500 curies, and the Swedish machine goes all the way down to 10 curies of activity. This means that some of these cobalt sources can be used 2 or 3 times. The cobalt is going to last through more than 1 half-life (cobalt 60 has a half-life of 5 years). From the small amount of experience we have, most therapists seem to want to replace their source at about 4 years; thus after 4 years a very high level source can be sold to a person who has a lower level machine. So some of these sources could be used twice.

The average number of curies that has gone into all of the current machines is about 1,000 curies. Most therapists are ordering this 1,000 curie device. This means, then, that we think we need something

like 6,000 of the 1,000 curie sources, or 6 million curies to keep all of the machines in operation. But since the hospital population can be expected to double in the next 10 years, this figure should be doubled. However, each of these sources lasts for about 4 years, and by throwing all of these assumptions together, my estimate of the number of curies of cobalt-60 that will be needed by 1961, will be something like 1 million curies with an increase to 3 to 5 million curies by 1966.

Then if we look at the planned goals for the production of cobalt 60, (exhibit 157, right) and increase this plan by what might be accomplished on short notice, we find that the United States could produce about half a million curies each year. The United States is also planning for the production of about 0.05 million curies (cobalt-60 equivalent) of cesium, which can be used in place of cobalt 60.

Representative COLE. What is that?

Dr. BRUCER. Cesium 137, is another isotope that can be used instead of cobalt 60. The Canadian production could possibly go up to 1 million curies a year, but they are planning a third of a million curies. The English production I am estimating at half a million curies possible, but they plan on only about 30,000 curies. We know nothing of the Japanese. They have not announced that they will produce any, and the Swedes will produce little, if any. The Norwegians production will probably be very small, the Italian production will be none, the Indian production I estimated at none, the South American production none, and the French production is unknown. I estimate a total of 30,000 curies from all other countries.

Representative PRICE. You have been talking about the requirements now for this cobalt 60 for the teletherapy sources for the next few years and so forth. Are you talking now only of the medical needs?

Dr. BRUCER. This is only for teletherapy.

Representative PRICE. And you are indicating a possibility of a serious shortage?

Dr. BRUCER. My estimate is that there is going to be a deficit in the production of cobalt for teletherapy sources only of something between 1 to 3 million curies. This is a deficit of what might reasonably be requested of the producers of cobalt 60.

Representative PRICE. Is anything being done to meet this problem? Does the Commisison have any plans for stepping up production or are there any recommendations made to the Commission on this point?

(NOTE.—Representative Price requested the AEC for a statement on its plans for the production of cobalt 60. Mr. Price's letter and the AEC reply will be found in the appendix on p. 367.)

Dr. BRUCER. I have informally recommended to the Commission that this production be increased.

Representative PRICE. How do you increase it? Do you need more reactors?

Dr. BRUCER. There would have to be more reactors, or at least more reactor space assigned to the medical production of cobalt.

Representative PRICE. How many reactors are assigned to that project right now?

Dr. BRUCER. I would prefer to have Dr. Dunham answer that.

Dr. DUNHAM. I believe only two are really producing large quantities of high specific activity cobalt to be used medically. The Brook-

haven pile, for instance, is putting out a great deal of low specific activity cobalt, which can be used commercially. Teletherapy cobalt 60 is rather special material that has to be made for medical use. It takes a relatively high flux reactor to do it. This is a real problem—how to squeeze more reactor time out of the available high flux reactors.

Senator BRICKER. Is this the reason Canada is able to produce more than we can, because of the special reactors that they have?

Dr. BRUCER. They have a couple of very high flux reactors now that do not have as much of their time preempted for other radiations. There is always a problem of priority.

Representative PRICE. Do you say that you have made some recommendations that would step up this program?

Dr. BRUCER. Yes; I have.

Representative PRICE. Are they formal recommendations?

Dr. BRUCER. Not a formal recommendation; no.

Representative PRICE. In what way would you suggest that it be stepped up? How would you go about it?

Dr. BRUCER. Every time a cobalt 60 source is sold in this country, everybody knows that this source is only useful for about 4 to 8 years. I think we are committing ourselves morally to maintaining that machine in operation every time we sell such a cobalt 60 source, since these machines, as I will show, are very expensive. We have already committed ourselves to future production of more sources.

I feel, therefore, that we should increase our production, if we are going to maintain this program at all, or at least maintain it for the people who already have purchased sources.

Senator BRICKER. What is the advantage of this type of teletherapy over electrically generated X-rays?

Dr. BRUCER. The therapy with cobalt 60 (and we have almost 3 years of experience with about 60 or 70 machines in operation) is that, first of all, there is less reaction of the skin to the therapy, and secondly, there is less discomfort to the patient in this kind of deep therapy. There is also a deeper penetration of this radiation into the body for deep-seated lesions. For these reasons, most of the therapists who have used cobalt 60 in preference to 250-kilovolt X-rays think it is a better kind of therapy. It does not produce more cures.

Senator BRICKER. Are the end results any different?

Dr. BRUCER. The end results in terms of cures are not much different, but the effect on the patient during the few years he lives is certainly an end result, and there seems to be much difference.

Senator BRICKER. The effects on the patient may have something to do with the end result.

Dr. BRUCER. That one factor probably has more to do with the popularity of this kind of therapy than the end result as measured in terms of number of cures.

Representative PATTERSON. Does a technician have to be trained especially for this kind of machine?

Dr. BRUCER. In most installations the technicians working with the 250-kilovolt electrical generators are also doing or are easily trained for cobalt 60 therapy.

Representative PATTERSON. Will these machines be in reach of our smaller hospitals throughout the country?

Dr. BRUCER. I have, on one of the later exhibits, a demonstration of how this is happening.

Representative COLE. Has the demand for cobalt 60 been greater than our supply?

Dr. BRUCER. I did not get your question.

Representative COLE. You anticipate a shortage. Does the shortage exist now?

Dr. BRUCER. The shortage has existed for the past few years. There have been more demands than we have been able to meet.

Representative COLE. By what factor, would you say?

Dr. BRUCER. I would say nobody has been denied cobalt, but they have had to wait for a source.

Representative COLE. You say the demand has been greater than the supply?

Dr. BRUCER. It has in that therapists have had to wait for from 6 months to a year and a half in order to get a source.

Representative COLE. They can anticipate their needs in advance, can they?

Dr. BRUCER. Yes; they can.

Representative COLE. Then nobody has been denied, but they may have had to wait.

Dr. BRUCER. Eventually, we hope, no qualified therapist will be denied a source.

Representative COLE. The shortage is not immediate, I judge. Or is it immediate?

Dr. BRUCER. Yes; I think there is an immediate shortage, and I think that there is a much greater future shortage of cobalt.

Representative COLE. Depending upon whether the people are going to make this large capital investment in the transition and to use the cobalt?

Dr. BRUCER. Yes, sir.

Representative COLE. Now you are going to get into that question?

Dr. BRUCER. I am going to get, not into the Commission's capital investment, but the hospitals' capital investment.

Representative PRICE. May I ask a question here? Has the Commission given any thought to the construction of a strictly medical high-flux reactor?

Dr. DUNHAM. They have not thought in terms of a specific reactor solely to produce high specific activity cobalt. The Commission is very much concerned with the problem of making more of this isotope available. They have tried up to now to use existing reactors, and any new high-flux reactor that becomes available to the Commission under its reactor program can be used for this purpose.

Representative PRICE. We are having increasing difficulty now getting the normal sources of supply from the existing reactors for the isotope program, the power program, the commercial program, and the weapons program. So that has not taken care of the situation that you are talking about here?

Dr. BRUCER. No, sir.

Dr. DUNHAM. It is a mater of priorities. That is where the problem comes?

Dr. BRUCER. Yes, sir. Before I leave these figures in your mind, I would like to read another set of figures, and these are estimates from Canada. By their investigation, they state that the United Kingdom

production (that is listed on exhibit 157 as England for half a million curies) is a possible prediction of about 30,000 curies per year. That is not the half million that I indicated was possible.

As you suggest, there is certainly a possibility that our own production (and this is quoted from a letter from the Canadian producers of cobalt 60), by 1958 and thereafter will exceed the figure of 300,000 curies mentioned in my letter to you. However, it would be necessary for us to take a different approach to the matter than that which we now have if this production were to particularly exceed 400,000 curies.

In other words, this estimate that I received from Canada is about half of my estimate of what they could do.

Representative COLE. May I inquire further about your figures there? You show a total anticipated need of about 2 million curies by 1966.

Dr. BRUCER. Yes, sir.

Representative COLE. That is an annual production, is it?

Dr. BRUCER. That is an annual production.

Representative COLE. But your total need by 1961 is 6 million.

Dr. BRUCER. Yes, sir.

Representative COLE. Then it would indicate that within 3 years after 1961 arrived, the total need will be met, if your annual production is 2 million and your total requirement is 6 million.

Dr. BRUCER. But one in a continuing yearly need. The other is an accumulated total.

Senator BRICKER. You have to multiply the 2 by 4?

Representative COLE. You do not consume the 6 million curies in 1 year's time?

Dr. BRUCER. No, sir. The cobalt 60 is consumed on a 4-year modulus and it decays on a 5-year modulus. Also, it must be remembered that there are other uses for cobalt besides teletherapy.

Representative COLE. I am just applying your own figures. This 6 million that you say is the need will be usable for a period of 4 years, will it not?

Dr. BRUCER. Yes, sir.

Representative COLE. So that you will not have to replace this 6 million until after that 4 years has expired.

Dr. BRUCER. Yes, sir.

Representative COLE. So that if your annual production is 2 million, then it would seem to me that very easily, the need will be filled by your production.

Dr. BRUCER. Yes, except for the fact that in these assumptions the one figure is for annual production, the other is for total accumulated need.

In these estimations I am also making the assumption that there is going to be an increase over this 6 million accumulated amount. There is an increased hospital population, and there is an increasing age, and an increase in the number of cancer patients, so that the need, I am predicting, is going to be about twice what it is now by 1966.

Senator BRICKER. Your 6,550,000 figure is the demand. That is now an estimated demand if all of the machines were converted to the new cobalt machines?

Dr. BRUCER. As of today, yes, sir.

Senator BRICKER. You have a slight period of conversion there in which you could catch up very easily to the current demand.

Dr. BRUCER. Since it takes approximately 2 years to make a cobalt source, I do not think that we can catch up very rapidly.

Senator BRICKER. But that will lessen the immediate demand for the cobalt 60.

Dr. BRUCER. Yes; it will if there is sufficient production.

Representative COLE. It takes 2 years to make a cobalt source?

Dr. BRUCER. Yes, sir.

Representative COLE. What do you mean by that?

Dr. BRUCER. When a piece of raw cobalt 59, ordinary stable cobalt, is prepared for irradiation it takes about 6 months to get priorities arranged and to get the source made and canned and loaded into the reactor. It stays in the reactor for a year. There is then another half a year after it comes out of the reactor, when it is being measured, and loaded, and shipped to various parts of the country. The average production lag is about 2 years.

Representative PRICE. Is there any way that this lag could be speeded up?

Dr. BRUCER. It could be speeded up at the tremendous cost of irradiating in exceedingly high flux reactors. I do not think that this is economically sound, but it does not have to be speeded up if we now start irradiating the cobalt for future production in the lower flux reactors.

Senator BRICKER. What about danger in the operation of these machines as compared with the conventional X-rays now?

Dr. BRUCER. Most of the therapists now using cobalt machines are using about the same procedures for the same conditions and with about the same relative facilities as those of the existing X-ray machines. There is not much change in procedure. There is merely a change in the energy of radiation.

One other important point goes along with these assumptions of production needs, and that is that the teletherapy sources are not the only way in which cobalt 60 is being used. One use, for example, in the Canadian production schedule is that the Canadians have already produced a few 10,000-curie sources, a few 20,000-curie sources, and they are prepared to produce a megacurie, or 1 million-curie source, as soon as somebody is willing to buy it. The United States has also produced some of these very large sources. These are industrial sources that are being used for such things as food sterilization, food pasteurization, chemical polymerization, irradiation of seeds, and so on. These industrial sources are much larger than the teletherapy sources, but they are produced in the same way and industrially they are used in a similar manner; therefore, they involve the same economic factors. They take away from the cobalt 60 teletherapy production. So this is another factor that enters into the estimates of how many curies are needed within the next 5 to 10 years.

Representative COLE. Are there a number of cobalt sources, and is there a great variety of cobalt sources?

Dr. BRUCER. Oh, yes. For example, in this country, there are two kinds of sources. We have the 1-centimeter wafers and the 2-centimeter wafers.

Representative COLE. Just a difference in shape?

Dr. BRUCER. Differences in shapes of the sources and differences in the amount and number of curies in the source.

Representative COLE. Then that is weight and volume. Is there any difference in the nature of the source?

Dr. BRUCER. No; the radiation is always the same.

Representative COLE. It is all cobalt 60?

Dr. BRUCER. Yes.

Representative COLE. When you speak of cobalt sources, you are referring to cobalt 60?

Dr. BRUCER. Yes, sir; cobalt 60.

Representative COLE. Which may be fabricated in different units of size and weight?

Dr. BRUCER. That is right.

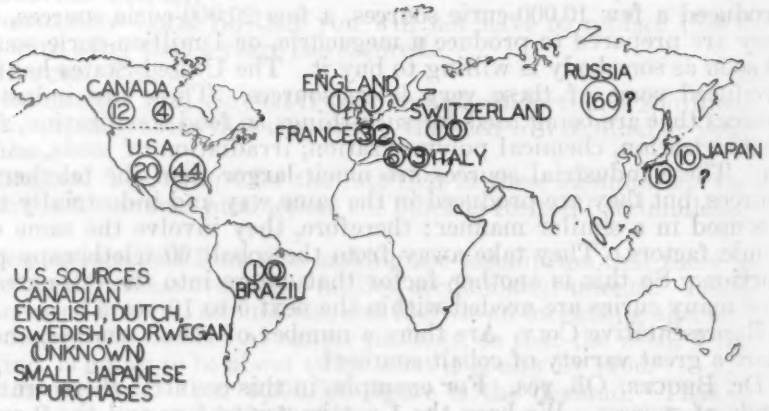
Representative COLE. But the content or nature of the content is the same.

Dr. BRUCER. The nature of the radiation is always the same. This is true 1-million-volt radiation.

Now I will show in exhibit 158 the distribution of the cobalt sources throughout the world. We cannot always tell which cobalt machines are used, but we assume that each of the cobalt sources is in a machine very similar to those that we showed in the previous exhibits. We show the Canadian sources that have already been produced and are now in operation in red, and the United States sources in blue. We find that there are 12 Canadian sources, and 4 United States sources in Canada now in operation. In the United States, we have 20 Canadian sources in machines in operation, and 44 United States sources.

EXHIBIT 158

WORLD DISTRIBUTION
OF COBALT 60 TELETHERAPY SOURCES
TO JUNE 1956



In Brazil we have one Canadian source and no United States source.

In England we have at least 1 Canadian source and at least 1 United States source in operation at the present time. There are quite a few English sources that I have not included on this chart.

In France we have 3 Canadian and 2 United States sources.

In Italy we have 6 Canadian and 3 United States sources.

In Switzerland, one Canadian and no United States sources.

In Japan we have approximately 10 Canadian and 10 United States sources in operation. But these are all in Japanese-made machines, so we are not quite sure, exactly, what the distribution of the sources are in the machines.

In the Soviet Union we have a statement by a Russian therapist in which he indicated that there were 160 sources either in operation or shortly will be in operation.

Exhibit 12 is a summary of how many sources there are. There are about 120 sources now in operation, whereas in 1950 there was only 1. So in a period of 5 years, we have had a very rapid increase in the use of cobalt 60 for teletherapy.

Representative COLE. Is it necessary to have a special machine to use the cobalt 60? Can you convert the old X-ray machine?

Dr. BRUCER. The old X-ray machines are very thinly shielded for a low-energy radiation. Cobalt 60 is a very high-energy radiation so the machine must be very thickly shielded, and, therefore, is very heavy. The ordinary 250-kilovolt X-ray machine weighs about 250 to 500 pounds. Some of the cobalt-60 machines are measured in terms of tons. Most weigh many hundreds of pounds. There is a big difference, and it is not a simple conversion.

To show about what the costs of these machines are to the hospital, on exhibit 159 we show a few of the first hospitals that had machines put into operation. Their costs are listed in terms of thousands of dollars.

EXHIBIT 159

THE COST OF COBALT 60 TELETHERAPY IN THE UNITED STATES

(IN THOUSANDS OF DOLLARS)

HOSPITAL	CURIES	SOURCE COST	MACHINE COST	INSTALLATION COST	TOTAL COST
CEDARS (L.A.)	1440	$88	$10	$42	$61
CITY OF HOPE (L.A.)	744	62	32	12	50
MEMORIAL (DETROIT)	341	22	20	16	38
LOUISVILLE GENERAL	979	80	20	4	32
PRIVATE (N.Y.C.)	306	18	20	10	32
UNIV. (LITTLE ROCK)	1089	90	20	.7	30
BELLEVUE (N.Y.C.)	599	46	20	.1	25
GASTON (MEMPHIS)	311	20	20	.9	23
PRIVATE (MEMPHIS)	309	20	20	.5	22
EMORY (ATLANTA)	294	28	10	2	15
AVERAGE COST IN 1956		$2 TO 20	$20 TO 30	$1 TO 50	$25 TO 100

The cost of the source, for example, in the City of Hope Hospital, which is an average-sized machine with a 744-curie source, was $6,200. The machine cost them $32,000 without the source, and the installation of the machine into the hospital—and they built a separate building—cost them $12,000. The total cost of their machine was about $50,000.

The exhibit shows nine other hospitals, and you see there is a wide variation in the costs of these materials. We can take the relative ranges and you find that cost of the source in most of the machines

ranges between $2,000 and $20,000. The cost of the machine in most of the hospitals is ranging between $20,000 and $30,000.

The cost of the installations range from very low cost—and this is where they have rooms already set up for supervoltage therapy—to very high cost. There are some later installations than these that have gone even higher than this $50,000. Thus, the total cost for most of the machines that are now in operation is ranging between $25,000 and $50,000.

Representative COLE. Does the cost of the source, or cost of the material have a standard price?

Dr. BRUCER. There is a standard price for cobalt 60.

Representative COLE. Does that figure, for instance, the second one on your exhibit there, for the City of Hope, does that represent the money paid to the Commission for the cobalt 60?

Dr. BRUCER. That was paid to the Commission for the irradiated cobalt, the source capsule, the loading of the cobalt into the source capsule; and a small portion of this, I think a couple of hundred dollars, was the transportation from Oak Ridge to Los Angeles.

Representative COLE. What is the unit price for cobalt 60?

Dr. BRUCER. The unit price changes with the specific activity, the number of curies per gram. For a very low specific activity, which is easy to produce, the cost is as low as $2 per curie. For a very high specific activity (many curies per gram of cobalt) it is as high as $12 to $15 per curie.

Representative COLE. What does the hospital consider when it determines the size of a machine that it will install?

Dr. BRUCER. There are many things. First of all, what cobalt 60 is available? Second, what rate of radiation is the therapist familiar with on his ordinary X-ray equipment? If the therapist is used to using a very fast machine, treating patients in 5 or 10 minutes, then he wants a very high activity source. If the therapist is used to using a low-speed machine, taking 20 to 30 minutes for treatment of the patient, then he usually wants one of the small sources. However, the biggest factor that goes into his decision is what kind of source he can get, and what is available at the time that he is ready to buy cobalt 60.

Senator BRICKER. There is no restriction on the machines available, and no limitation on the machines?

Dr. BRUCER. The machines are being made commercially in this country by four companies now, and anybody can buy one.

Senator BRICKER. You can get them delivered within a reasonable time; 4 or 5 months?

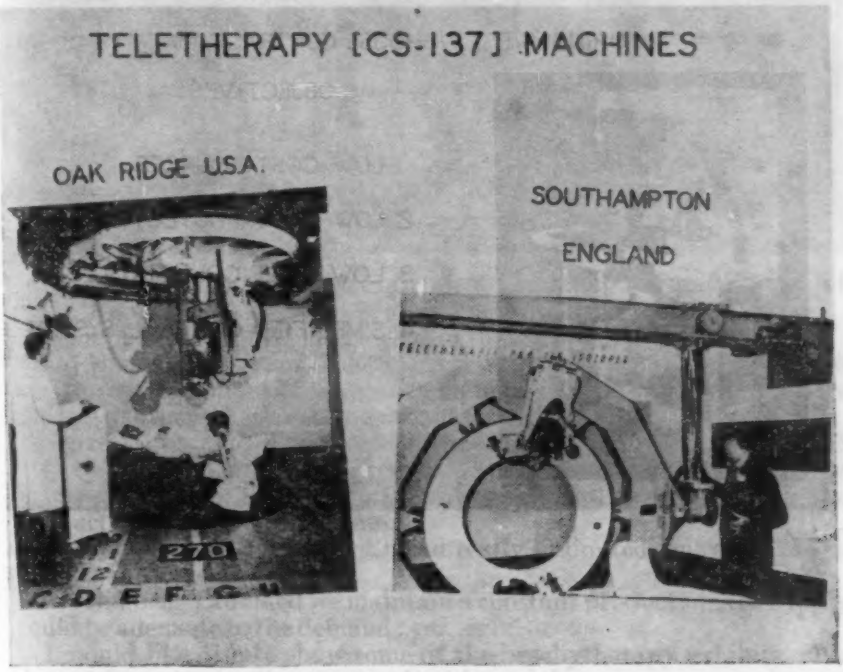
Dr. BRUCER. Less than that.

Senator BRICKER. Less than that?

Dr. BRUCER. Yes. Within a month you could have machines delivered, but it is no use having the machine unless you have the source for it, so the source production is the thing that holds up the program. Probably it always will.

We also have another radiation source, and this is cesium 137. This source material should be more economical since it is a waste product of the nuclear reactors, and since every time a reactor is built we make cesium. The only problem here is the separation of the cesium from the reactor fuel. It has about the same usefulness and so it can be used for teletherapy. So far, two machines have been made for cesium 137. A machine in Oak Ridge, and a machine in Southampton, England, have been made to use the cesium 137 source. England is making about 30 cesium 137 sources and we are preparing to make many additional sources in this country (see exhibit 160).

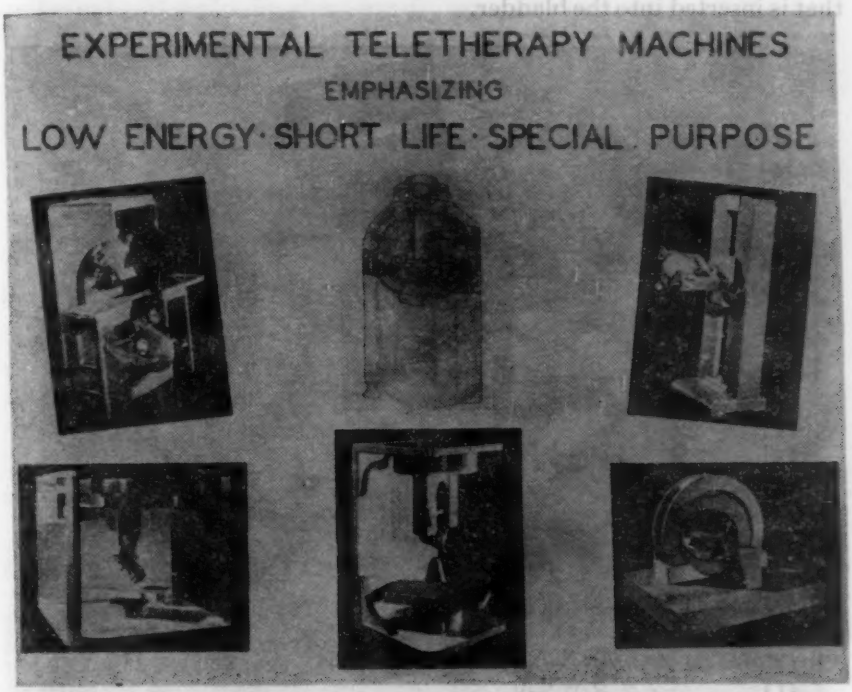
EXHIBIT 160



There are lots of other sources that could be used. Cobalt 60 is not the only one. We can use cesium, we could use europium, and we could use some of the very low-energy sources. We have other possibilities that should be or are being thought of in this program. One is the very low energy isotopes; another is the short-lived isotopes. Machines can be made for special purposes. Exhibit 161 shows the objectives of a current contract we have with the Westinghouse Co. Exhibit 162 shows some of the models of some of the machines that have been proposed for development in the next few years.

EXHIBIT 161

EXHIBIT 162



Senator BRICKER. Those are other isotopes, using cesium and cobalt?

Dr. BRUCER. Other isotopes, other energies, and other purposes.

Senator BRICKER. What are some of the other isotopes?

Dr. BRUCER. Cesium 137 is the main one, and europium 152 and 155 are others. Salenium 75 is another, cadmium 109 is another, and there are lots of others that are being considered.

Senator BRICKER. They could be produced in unlimited quantities?

Dr. BRUCER. They can be produced, not in unlimited quantities, but in very large quantities, with the same facilities that we use for the production of cobalt and cesium.

Senator BRICKER. I did not mean really unlimited, but adequate to the demand.

Dr. BRUCER. Provided we maintain a constant production, the supply could be adequate to the demand; yes, sir.

I would like also to show some of the brachytherapy exhibits. We do not have to use thousands of curies in therapy; we can also use thousandths of curies by putting the source very close to the tumor. These are called, not teletherapy but brachytherapy devices. There are many kinds of brachytherapy devices. This device, shown at the left on exhibit 163, is a gun to inject small seeds into a tumor. It reached the peak of its development in England. The first one is a German machine and the last one is an American adaptation of the same device. The top picture is of a German device that uses very small beads that can be put into the bladder. The one on the right is

from Switzerland, showing the use of liquid isotopes put into a balloon that is inserted into the bladder.

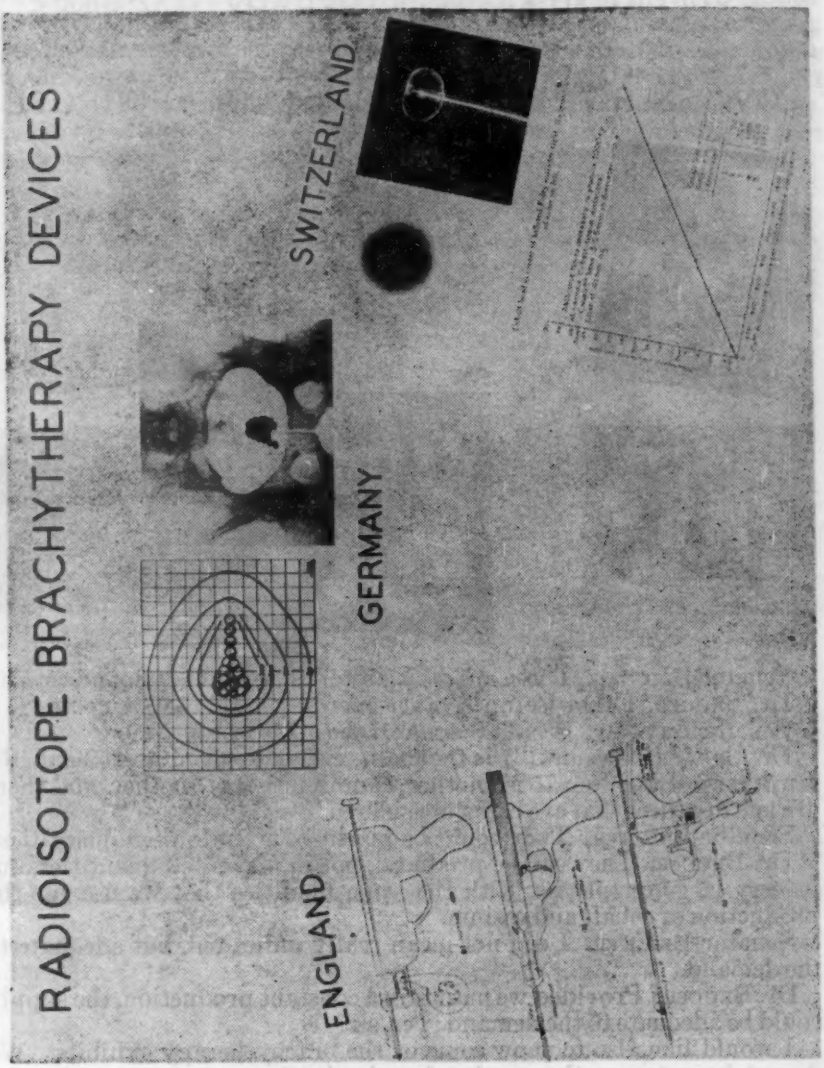


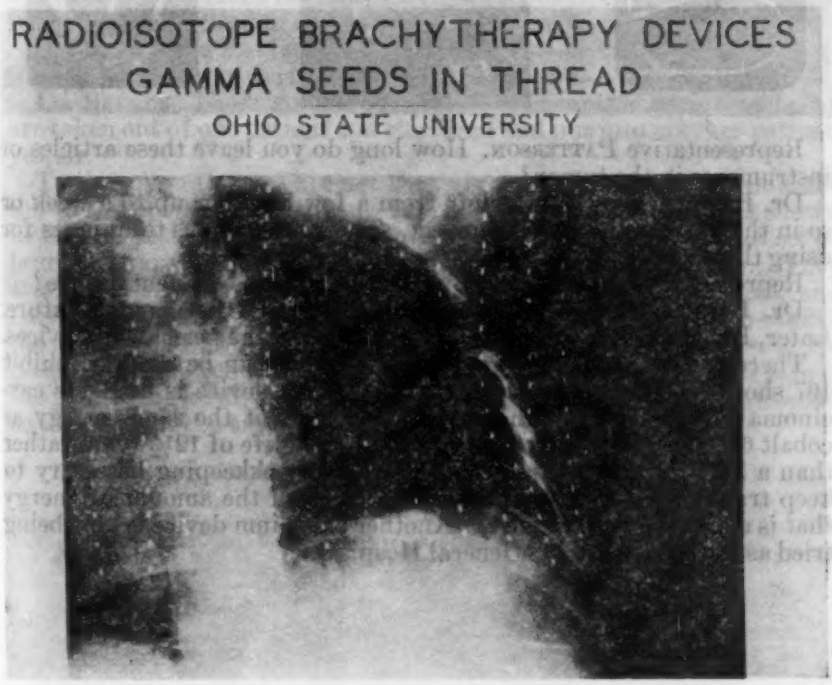
EXHIBIT 163

There are other ways of placing the source close to the tumor. As shown on exhibit 164, you can absorb some of a liquid isotope onto a surgical sponge. In New Orleans there is one surgeon that is trying this. Exhibit 164 does not mean very much to you, but it shows a part of a dog into which a piece of surgical sponge was inserted. The isotope stayed in place very well. It shows a method of getting an isotope into place with some assurance that it will stay where it was put. It will stay there for the length of life of the isotope.

Another kind of device puts cobalt seeds into nylon thread. This thread is then sewed into a tumor of the breast as shown in the X-ray in exhibit 165.

EXHIBIT 164

EXHIBIT 165



Devices that we have spent a great deal of time developing (since they can be produced rather easily) are made of cobalt 60 in an alloy as shown on exhibit 166. When cobalt 60 is put into a corrosion-resistant alloy—this is one of the International Nickel Co.'s corrosion-resistant alloys—we can then machine any shape of device—needles, seeds, beads, and small cups that are put behind the eyeball surgically. Anything that a surgeon can think up is possible to produce.

EXHIBIT 166

Representative PATTERSON. How long do you leave these articles or instruments in the tumor?

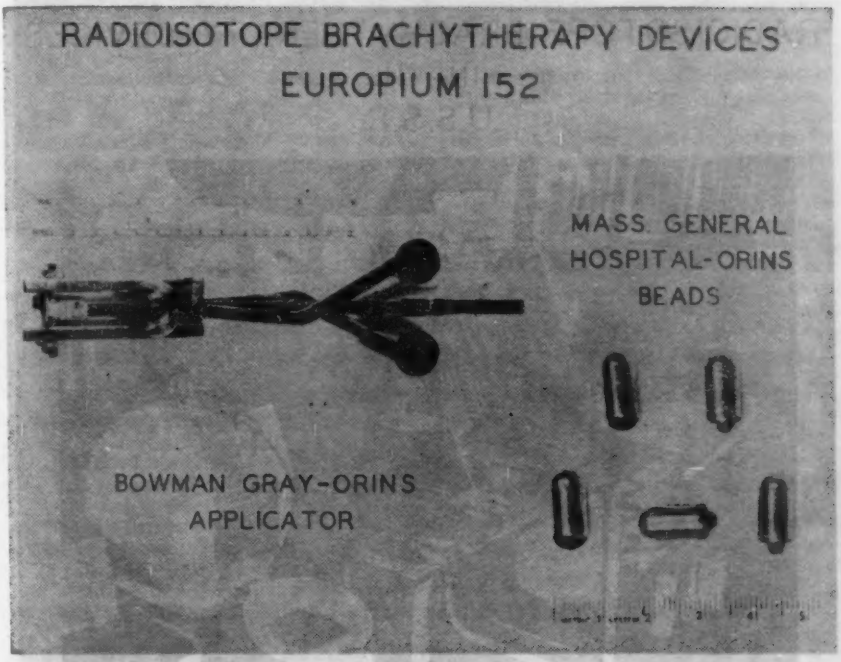
Dr. BRUCER. They can be left from a few hours or up to a week or so in the patient and then removed. There are various techniques for using these devices.

Representative PATTERSON. But they are not a permanent fixture?

Dr. BRUCER. No, sir. They do not become a permanent fixture. Later, Dr. Harper is going to show you some of the permanent devices.

There are other isotopes besides cobalt that can be used. Exhibit 167 shows one that uses europium 152. This device is used for carcinoma of the cervix. The europium has about the same energy as cobalt 60, except that europium 152 has a half-life of 12½ years rather than a half-life of 5 years. Therefore, the bookkeeping necessary to keep track of this source and keeping track of the amount of energy that is emitted is much easier. Another europium device is now being tried as the Massachusetts General Hospital.

EXHIBIT 167



Senator BRICKER. Why couldn't the X-ray machine, deep therapy, be used?

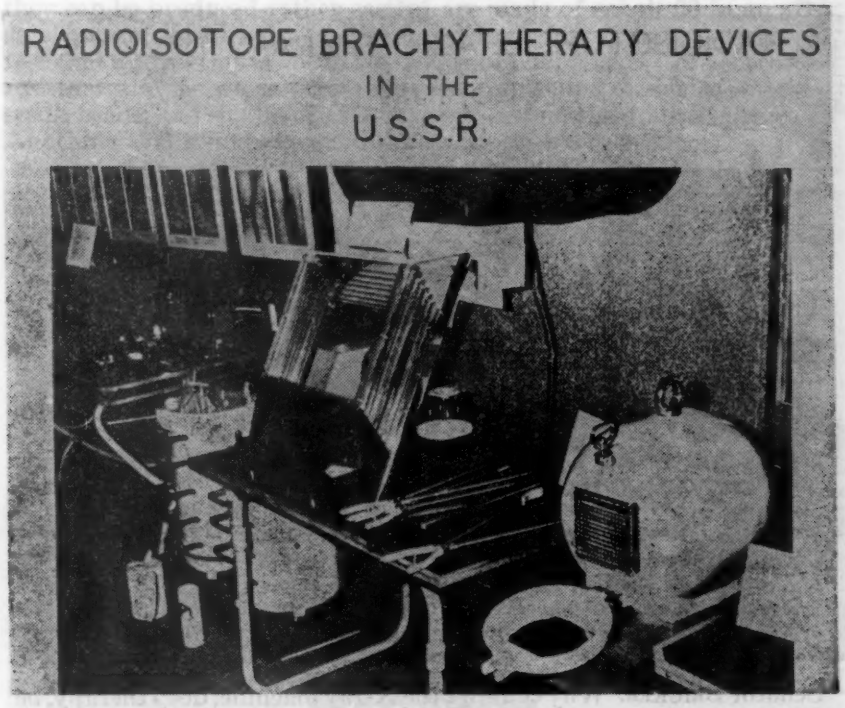
Dr. BRUCER. I think the best answer is that the radiotherapist chooses to operate very close to the tumor rather than through normal tissue.

Representative PATTERSON. Can the isotope be taken from one person and then used in the next patient?

Dr. BRUCER. These isotopes are all in sealed capsule sources and they are taken out of one patient and sterilized and put into another patient, yes, sir.

To show you that we are not the only ones that do this, exhibit 168 shows the brachytherapy setup that has been devised and was shown in Geneva last summer by the Soviet Union. They have put a set of brachytherapy devices into each of their cancer therapy centers. They are not using many different kinds of brachytherapy devices, and they are apparently using only the needle-shaped device. The exhibit shows a cobalt 60 safe, with many drawers. They use about 180 needles in each set which are kept in this safe. Next to this safe is the gadget for loading the needles and tubes and getting them threaded so that they can be used by the surgeons.

EXHIBIT 168



Since I have already used up much more than my allotted time, I think that I had better stop.

Representative PRICE. We are kind of rushed for time here today, and we would like to have an inclusion in the record of many of these charts with an explanation.

Dr. BRUCER. I will write an explanation of the additional exhibits that will be put in the record.

Representative PRICE. That will be fine.

Thank you very much for a very interesting presentation. It was very well done.

(The information referred to follows:)

One other program should be brought to the attention of the committee. This is the program on thyroid radioiodine uptake calibration.

When we speak of the number of curies of activity that are being used by the medical profession, then cobalt 60 is probably the most important isotope. However, if we talk in terms of the number of patients that come in contact with an isotope for medical purposes, then radioactive iodine is the most important.

About two-thirds of the isotope shipments that leave Oak Ridge are shipments of radioactive iodine to some medical institution for the purpose of either diagnostic or therapeutic use by some physician. It has been estimated that approximately 2,000 physicians in the United States are either using radioactive iodine or have access to its use.

The introduction of radioactive iodine to the general medical profession in 1946 was followed by a development of many kinds of measuring equipment. Shortly after the open reactor production and distribution of iodine 131 by the Atomic Energy Commission, it was found that scientists in different sections of the world were using different assumptions and different measuring tools and could not match each other's calibrations. When a bottle labeled as 1 millicurie of radioactive iodine was shipped from Oak Ridge to 1 scientist he might have measured the shipment as 2 millicuries or he might have measured the shipment as one-half millicurie. With intensive effort by the Atomic Energy Commission, the National Bureau of Standards, and individual scientists throughout the world, the problems of calibrating a uniform sample of iodine 131 were solved and since 1950 a sample of iodine 131 could be accurately calibrated in most physical and medical laboratories then in operation.

This made the dagnostic use of iodine 131 a highly desirable clinical tool. A furious development of instruments followed in the years immediately after 1950 to make the clinical measurement of radioactive iodine as simple, as direct, and as laborsaving as possible. Along with this development the number of physicians using iodine 131 increased rapidly and some of these physicians were not highly skilled technicians in physics. It was gradually realized that the physical measurement of a point source of iodine 131 was not the same as the clinical measurement of the iodine 131 uptake in the thyroid gland. Certain biological sources of therapy became apparent. The results of some clinical determinations were found not to match the results of the same clinical determinations in other clinical laboratories. In many of the larger hospitals this lack of calibration did not really matter since the larger hospitals are running their own controlled experiments and were determining calibration factors for the particular instrumentation currently in use. However, most of the iodine usage is not in large hospital laboratories; it is in the hands of relatively small users that must follow the recommendations of large laboratories.

By 1953 a few physicians and physicists realized that the reputation for physical precision in the measurement of iodine 131 might not be warranted in clinical measurement. It was easily observable in the literature that iodine 131 uptake measurements as reported by various clinical laboratories were not identical. A small group of internists and physicists met in Oak Ridge in 1954 to discuss this question of interlaboratory variations of thyroid uptake. The decision at this meeting was that one of the major reasons for variation and inaccuracy was the absence of a suitable check standard that would allow for an intercalibration under conditions closely simulating measurements in the human patient. At this meeting a simulated iodine 131 gamma-ray standard was presented and a program was set up by the committee to answer a number of questions.

First, is there sufficient variation in thyroid uptake measurements as performed clinically to warrant concern? Second, can the various methods of measuring thyroid uptake be intercalibrated? Third, how should this intercalibration be done?

To answer these questions a three-phase program was started in Oak Ridge. The first phase was to make a series of calibration mannequins that closely

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simulated human patients with radioactive iodine. Exhibit 169 shows 6 of the 9 mannequins that have been made. In exhibit 170 there is shown an X-ray

EXHIBIT 169

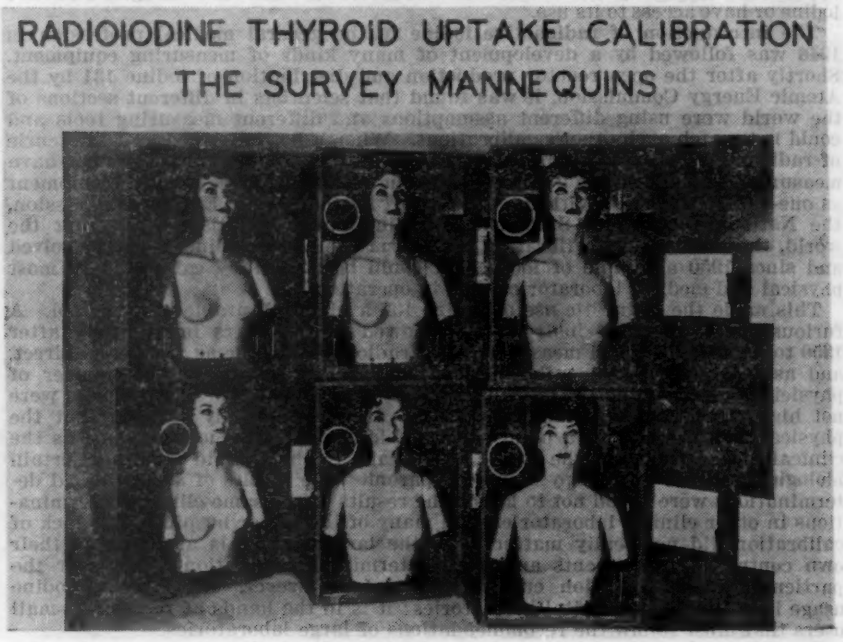
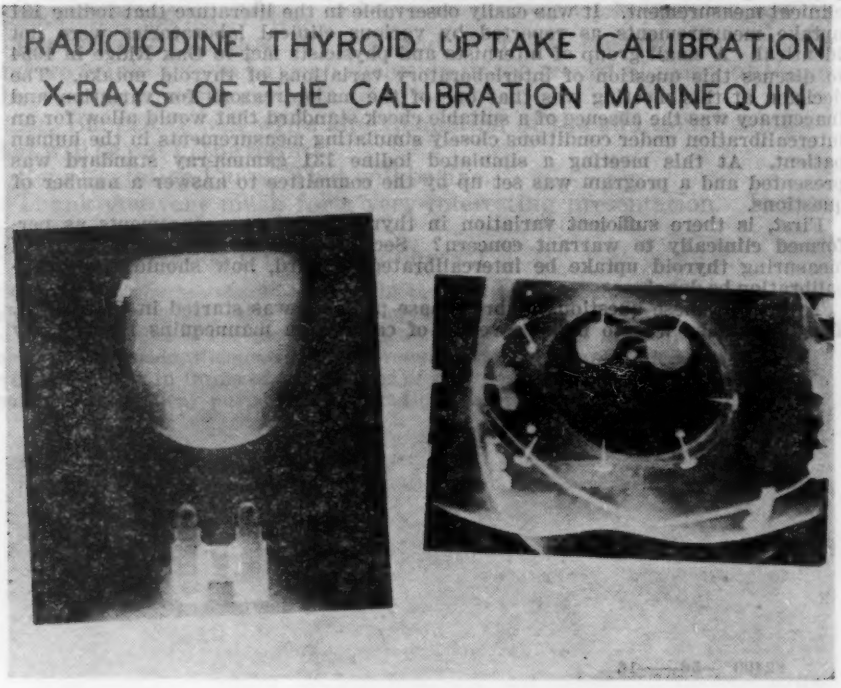


EXHIBIT 170

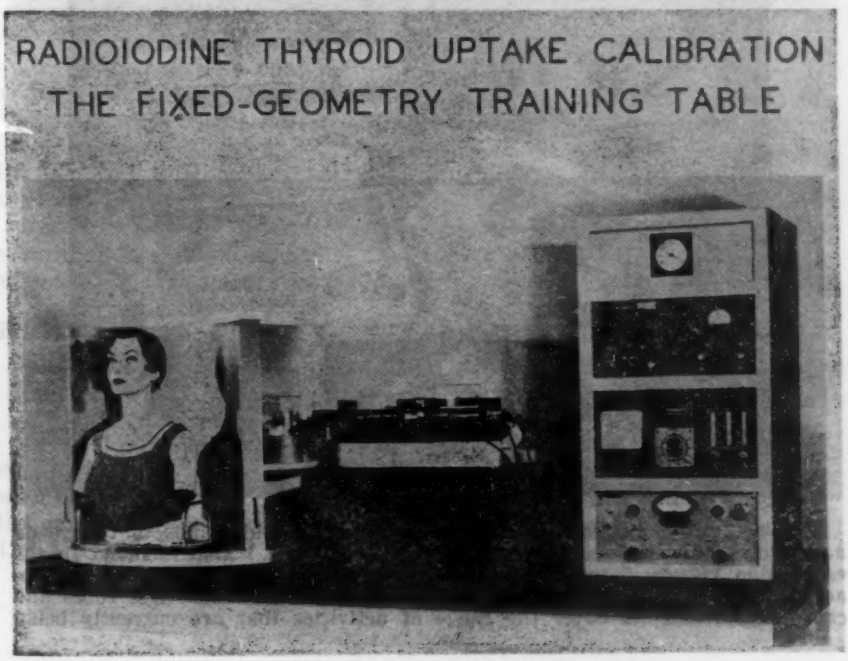


from the front and an X-ray through the top of one of these mannequins. These X-rays show the position in the mannequin of a simulated thyroid gland made of babbitt metal. The thyroid gland is filled with a substance called mock-iodine. Mock-iodine is a mixture of two other isotopes—barium 133 and cesium 137—which give off a gamma-ray emission closely simulating that of iodine 131. However, whereas iodine has a half-life of 8 days and thus cannot be used for intercalibrations throughout the world, mock-iodine has a useful life of approximately 10 years; it can be deposited in the mannequin so that it simulates the distribution of radioactive iodine through the body of a real patient.

A number of the mannequins are made to simulate the kind of gamma-ray emission one would expect to find in a hyperthyroid patient. Some of the mannequins are made so that they will simulate the gamma-ray emission that would be found in a patient with a normal thyroid gland. Two of the mannequins were made to simulate the gamma-ray conditions that would be found in a hypothyroid patient. These mannequins were then sent to six medical centers throughout the United States and to the Veterans' Administration hospitals. From these medical centers the mannequins were sent to approximately 160 medical laboratories using radioactive iodine for diagnostic tests in the United States and in England. Each of the laboratories made a measurement with its own quipment of the uptake of mock-iodine in the simulated patient. The results are now being gathered by the committee. It has been demonstrated that there is a sufficient variation in the methods and in the results to warrant considerable concern over the accuracy of this method of measuring a physiological function. An attempt is now being made to extend this survey so that eventually it will reach all of the laboratories who care to participate in the calibration of their methods.

It is not sufficient just to demonstrate that there is some error in the methods. It is also necessary to determine why there is error in the methods and to attempt to correct these errors. In exhibit 171 we show a picture of the fixed-geometry training table that has been set up in Oak Ridge to study the effects of variation of physical techniques in measuring radioactive iodine. This training table has a simulated patient and a number of simulated standards on a rotating platform that is indexed to come to rest in fixed positions. Also on the table you can see a number of different methods of measuring thyroid

EXHIBIT 171

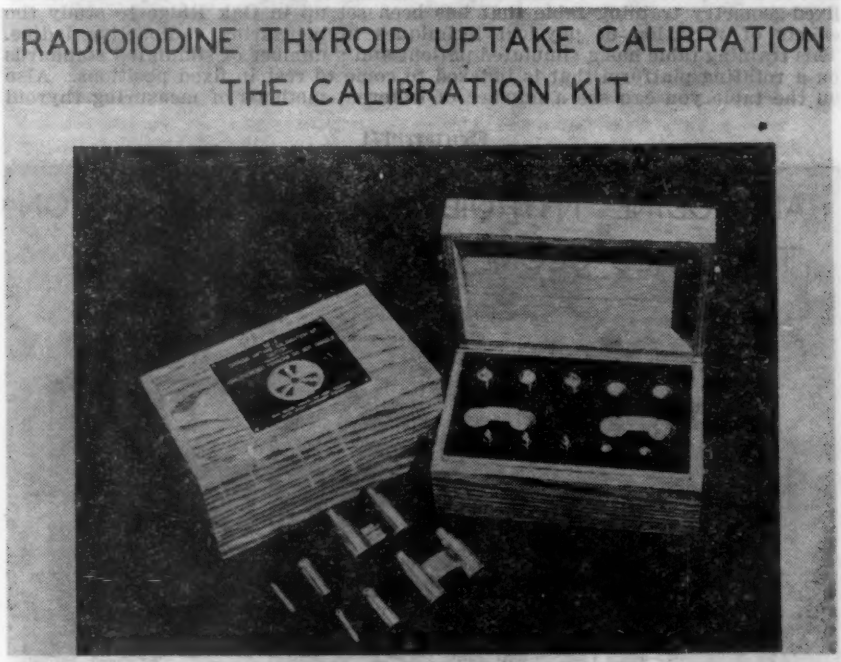


uptake. One is a Geiger-Muller tube method, one is a scintillation crystal method, and the third is a new spectrometer method. Each of these methods has its own counting circuit independent of the other methods of doing the measurement. By using this training table the student of thyroid uptake measurements can duplicate the geometry and physical factors in his own technique and can have demonstrated for him the variations that occur with collimation changes, filtration changes, and changes in distance and other physical factors of measurement.

The second phase of the thyroid radioiodine uptake calibration program is to allow physicians that are using radioiodine to come to Oak Ridge and study some of the reasons for the variations in clinical results. The second phase of the thyroid uptake calibration program is now being prepared; it will start during the week of September 24 with the formal opening of a series of working conferences that will eventually be opened to all physicians using radioactive iodine.

However, if it is not sufficient just to demonstrate an error, neither is it sufficient to demonstrate why the error occurs. The thyroid uptake calibration committee feels that a further step is necessary and that it is necessary to devise some method whereby each individual physician could calibrate his own equipment and eventually get the same answers with his own technique that other persons get with widely varying techniques of measurement. For this reason a third phase of the program is now being started. This third phase will consist of the sending out to as many physicians as possible a calibration kit that will allow each physician to calibrate his own equipment and his own methods. The calibration kit that is now being studied by a few of the larger clinical laboratories is shown in exhibit 172.

EXHIBIT 172



This calibration kit consists of two simulated thyroid glands that have an accurately calibrated amount of mock-iodine in them. Also included in the calibration kit are 5 test-tube size samples with varying amounts of radioactive iodine and 5 simulated capsules of mock-iodine. These test tubes and capsule-sized samples cover the range of activities that are currently being

used by physicians as the dose of iodine given to the patient. The National Bureau of Standards in the United States, the National Physical Laboratories in England, and the National Physical Laboratory in Germany have cooperated with the thyroid uptake calibration committee in performing intercalibration of the mock-iodine standards.

This calibration kit is not yet perfected; there is still a slightly different gamma-ray emission from the calibration kit than there is from a patient who has been given radioactive iodine. However, the method of perfecting the calibration kit is now known and as soon as the experiments are completed a sufficient number of calibration kits will be made so that a calibration survey can be started. Therefore, within the next 2 years we expect to be able to distribute calibration kits throughout the world as rapidly as feasible and allow each individual clinical laboratory using radioactive iodine to calibrate its own equipment so that it gets the same answers as every other laboratory.

It might sound from the results of the survey that all of the work that has previously been done with radioactive iodine is an error. Such an interpretation is not true. Almost all of the laboratories that are now using radioactive iodine have established their own normal ranges following the characteristics of their own measurement machinery. Therefore, the answers they get on individual patients are adequate within their own laboratories. The diagnoses they make from the laboratory tests are not necessarily affected by these errors. However, the people doing these measurements cannot talk to scientists in other laboratories and cannot compare their results with other laboratories. For these reasons, although their diagnoses have an adequate immediate accuracy, the inaccuracy of intercalibration between laboratories is holding up the progress of the development of radioactive iodine techniques. There are many other tests that could be performed and that might be developed but are held back by the inaccuracy of intercalibration.

The thyroid uptake calibration program is getting our first priority efforts at the present time to correct this inaccuracy of intercalibration and to allow for the normal progress of radioiodine techniques in clinical practice. The thyroid uptake calibration program will be a difficult and slow program. It demands the close cooperation of hundreds of scientists throughout many Government and private laboratories. Since the program involves the use of fairly large amounts of expensive equipment and many tediously calibrated standards, the program must of necessity progress slowly. However, before many years have passed we expect to allow any physician who wishes to participate to cooperate in the intercalibration of his own clinical measurements.

Dr. DUNHAM. The next medical scientist to present a report will be Dr. Lee Edward Farr, Chairman of the Medical Department of the Brookhaven National Laboratory. Dr. Farr will discuss Neutron Capture Teletherapy, and bring you up to date on the activities at Brookhaven, with which you are familiar to a considerable degree, anyway.

Representative PRICE. We are glad to welcome you before the committee. We have had the opportunity of being with you on other occasions in Brookhaven and in Geneva.

STATEMENT OF DR. LEE EDWARD FARR, CHAIRMAN OF THE MEDICAL DEPARTMENT, BROOKHAVEN NATIONAL LABORATORY

Dr. FARR. Mr. Chairman, 2 years ago I had the privilege of discussing the medical program at Brookhaven National Laboratory with this committee. We have since that time continued work along the general lines of endeavor set forth at that hearing (exhibits 173, 174, 175, 176, 177, and 178).

EXHIBIT 173. An outline representation of the medical research program at Brookhaven. Although neutron capture therapy is shown as a major subdivision it is apparent that data obtained in all other fields of endeavor is also very pertinent to this special field of work.

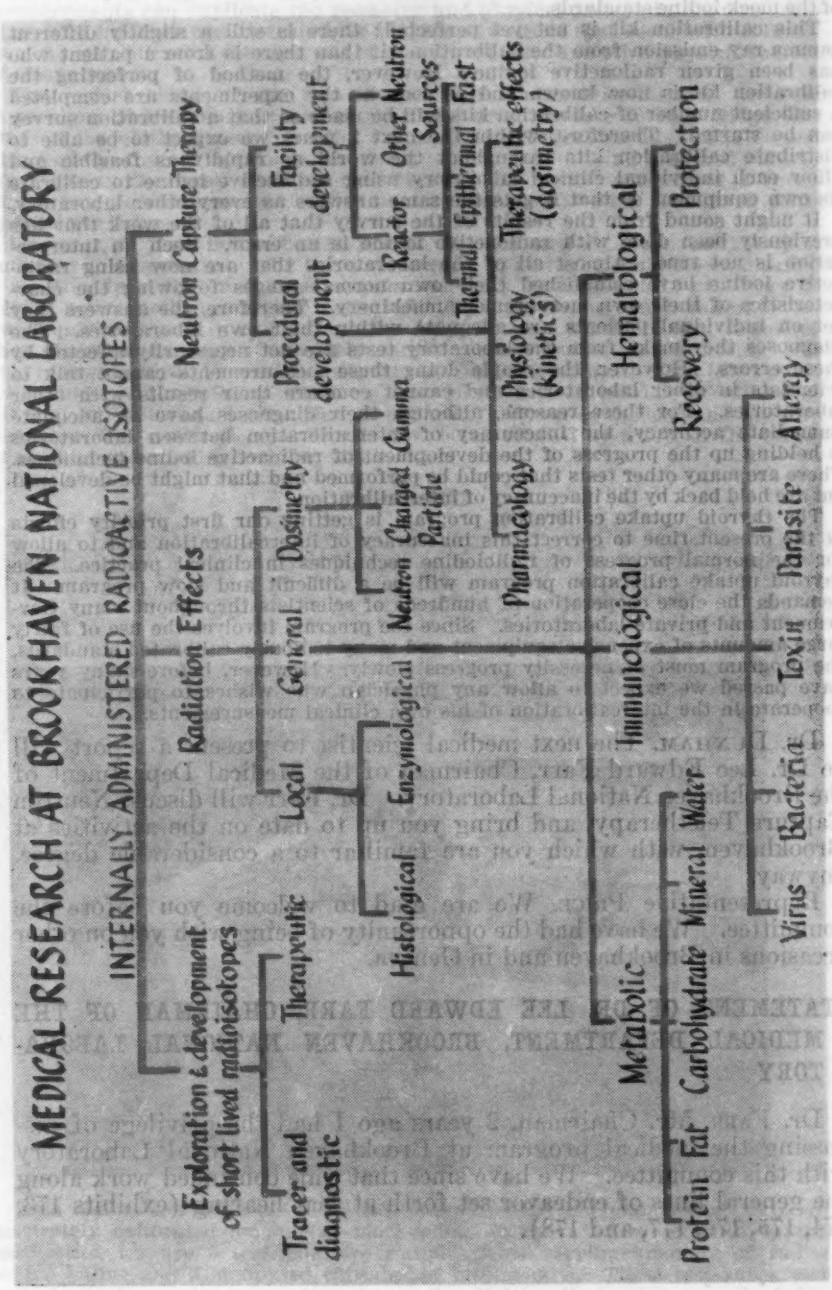


EXHIBIT 174. Schematic representation of effects of thermal neutron capture by boron 10 with almost instantaneous disintegration into an alpha particle and a lithium atom.

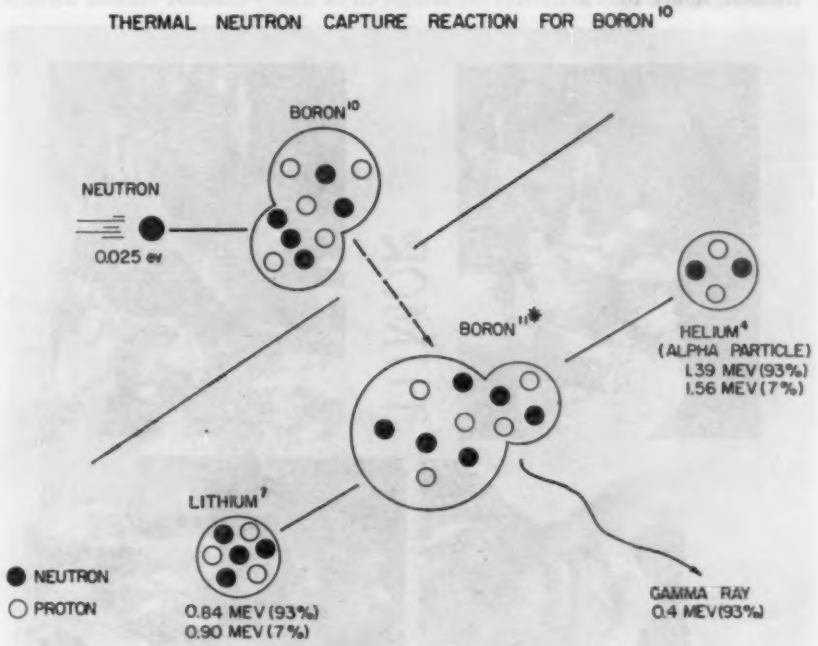


EXHIBIT 175. Pictures of actual treatments at present reactor facility. The cramped quarters and general lack of accessibility to the treatment port should be contrasted with facilities to be provided in Brookhaven Medical Reactor, figure 10.

EXHIBIT 176. Schematic representation of neutron capture therapy. Upon completion of intravenous injection of boron compound (time, zero), patient is positioned over reactor port to that distance from port to tumor is minimal. Reactor shutter remains closed so no significant radiation exposure occurs.

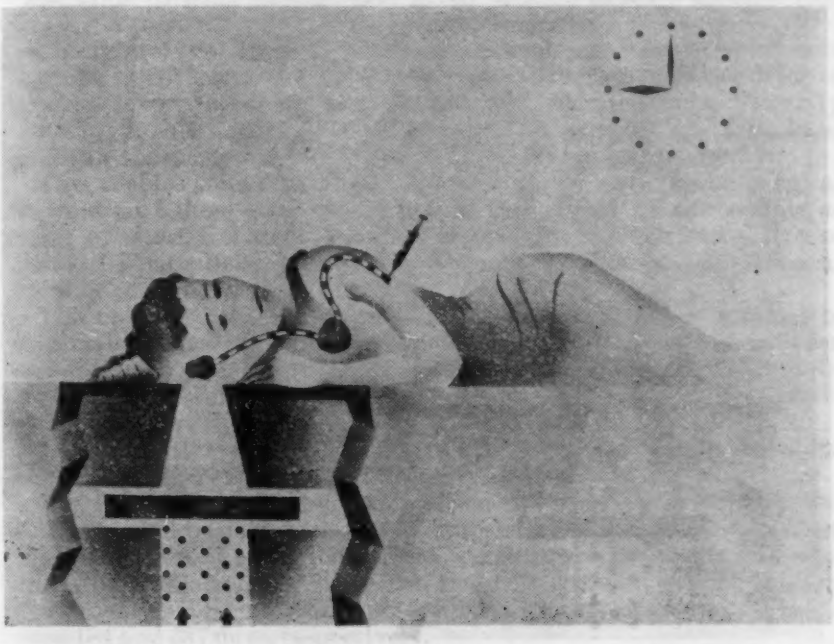


EXHIBIT 177. Schematic representation of neutron capture therapy. Exactly 8 minutes after completion of boron compound injection the shutter is opened and thermal neutron exposure begins.

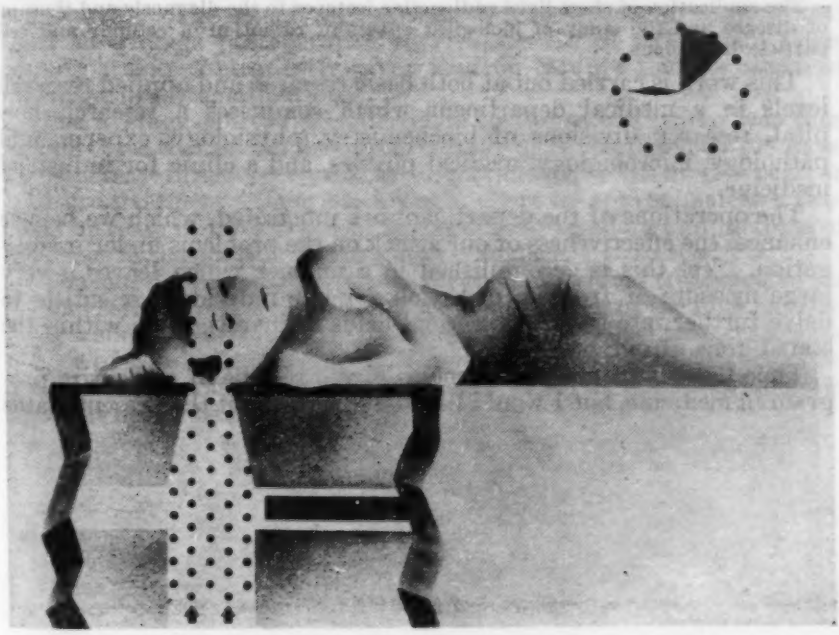
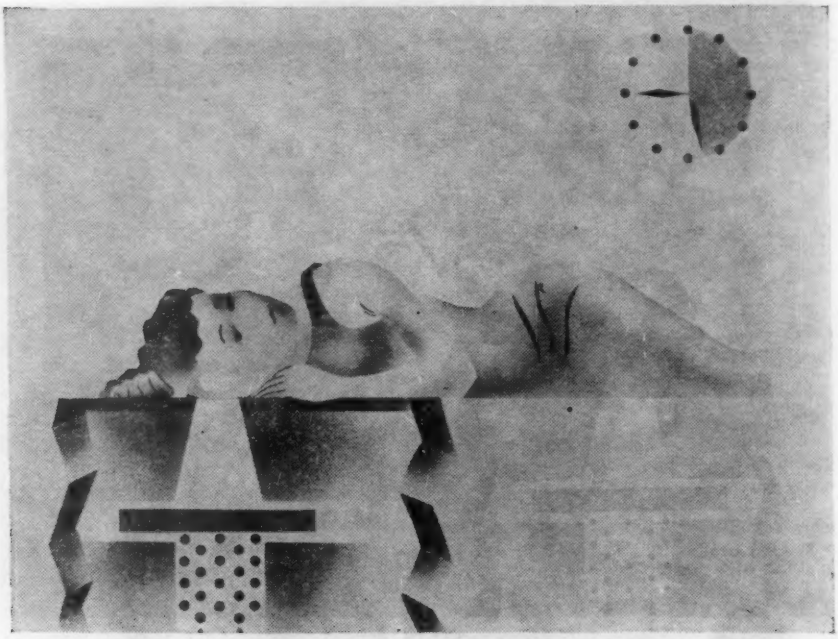


EXHIBIT 178. Schematic representation of neutron capture therapy. Twenty minutes after radiation has begun with thermal neutrons the shutter is closed. The treatment thereby is concluded and the patient is ready to return to the hospital.



To refresh your memory, the basic objective of the medical program at Brookhaven can be succinctly stated as:

The application of short-lived radioactive isotopes to the diagnosis and therapy of disease and the study of biological effects of radiation of cellular and cell particle dimensions.

This work is carried out at both basic research and applied research levels in a medical department which comprises a research hospital, research divisions of biochemistry, physiology, experimental pathology, microbiology, medical physics, and a clinic for industrial medicine.

The operations of the department are integrated, which we believe enhances the effectiveness of our attack on the problems under investigation. Yet this is accomplished in a manner which leaves a very large measure of freedom of action for our individual scientists to delve further into their own special fields of investigation within the stated aims of our program.

Time today will not permit me to give a résumé of our entire program in medicine, but I would like to tell you about the present status

of neutron capture therapy. First, of course, are the results of treatment to date. In the first series of 10 patients treated the average survival from operation by neurosurgeon to death was 189 days, and these same patients subsequently given neutron capture therapy survived 108 days after the radiation treatment.

The figure we believe to be the significant one in this instance is that of days of survival postneutron capture therapy. Since prior to treatment with neutrons each patient was operated upon to verify tumor type histologically and in most instances to effect surgical removal, the postoperative survival is given for comparison.

This enables comparison with other available statistics on surgical treatment of these tumors to establish uniformity of our sample as being of short life expectancy without further treatment. It also shows the patients were in a relatively uniform serious condition at the time of radiation.

The operative procedure in both groups varied from minimal to maximal removal of visible tumor. The difference in time between postoperative survival and postneutron radiation survival reflects the period which intervened between surgical treatment and postoperative neutron capture therapy.

Representative COLE. What were the extremes? What were the outer limits there?

Dr. FARR. The maximum time from operation to treatment was 1,359 days in 1 patient, and the minimum was 14, the average was about 45 days—between operation and neutron capture therapy. The minimum postradiation survivals in series 1 and 2 were 41 and 93 days, respectively. The maximum postradiation survivals in series 1 and 2 were 184 and 337 days, respectively.

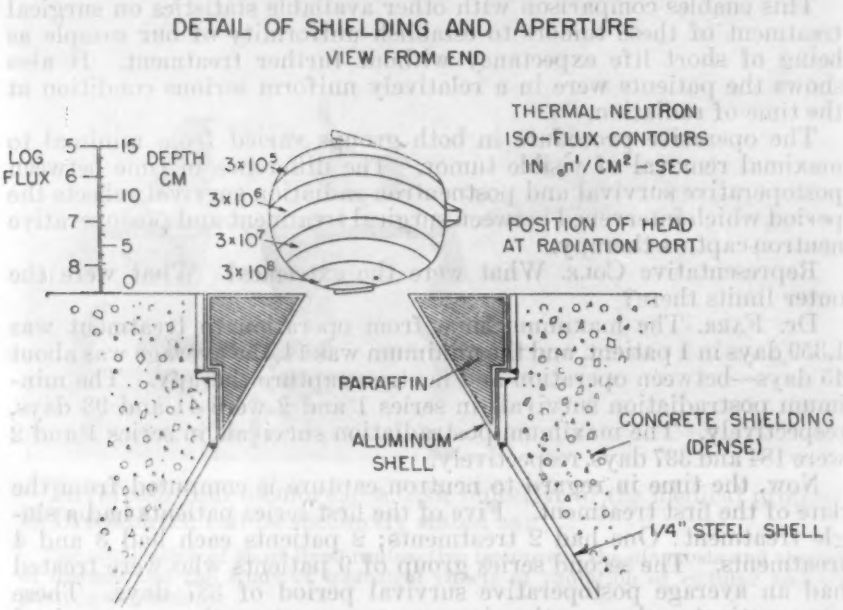
Now, the time in regard to neutron capture is computed from the date of the first treatment. Five of the first series patients had a single treatment: One had 2 treatments; 2 patients each had 3 and 4 treatments. The second series group of 9 patients who were treated had an average postoperative survival period of 387 days. These same patients subsequently given neutron capture therapy survived 191 days after the radiation.

The average postradiation survival of the second group was then about twice that of the first group or 191 days compared to 108 days. The increase in survival, we believe, was due to a more effective neutron capture treatment. This was brought about by approximately a twofold increase in the amount of boron administered and an increase of 30 times in the neutron flux at the skin surface.

The length of neutron exposure for each individual treatment in the second series was one-half that of the first. Seven of the nine received only a single treatment and two patients each received two treatments. Those of us who have participated in this work believe that these results are encouraging while we are well aware of their shortcomings in what might be hoped for.

It became obvious to us early during the treatments of the first series of patients that both neutron flux (exhibit 179) and boron dosage were inadequate to produce the results desired. Consequently, following completion of the first patient series the medical facility at the Brookhaven research reactor was modified extensively (exhibit 180).

EXHIBIT 179. Thermal neutron isoflux contours in average head. Data obtained by gold wire activation in patients and by tissue equivalent phantoms. Values shown are for an incident thermal neutron flux upon the skin 3×10^8 neutrons per square centimeter per second. For adequate midline therapy an incident flux of 10^{11} neutrons per square centimeter per second would be required.

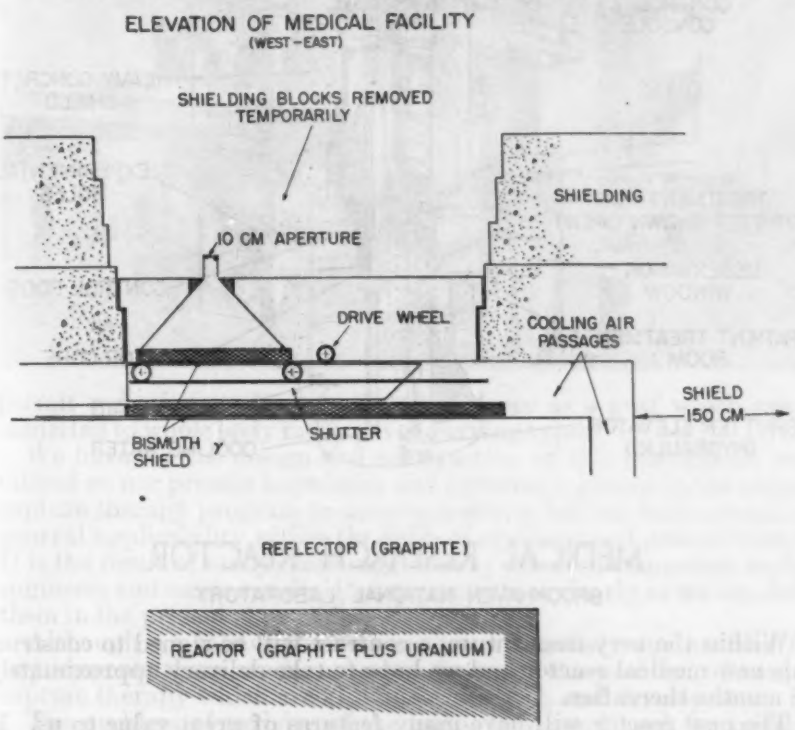


By such means, we increased the flux some 30 times and by introduction of a shutter, we effected other operating improvements in the use of the facility. It was apparent, however, that this modification was inadequate for ultimate needs even before the second series of patients was started. So over 3 years ago, we began to draw up some medical operating specifications which another nuclear reactor might satisfy and which would be especially useful for neutron capture therapy.

Before embarking on a reactor design, the possibility of obtaining an adequate thermal neutron flux from accelerators or fixed sources of radioactive isotopes was investigated for us under contract by Advance Technology Corp., of White Plains, N. Y. Their conclusion in which the Brookhaven physicists and engineers concurred, was that a nuclear reactor provided the only practical source of required neutron flux at this time.

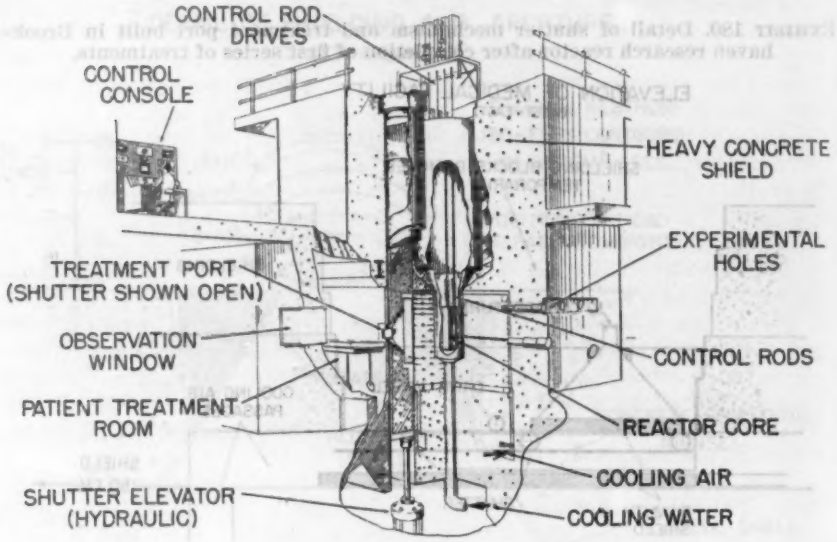
Subsequently a conceptual design was worked out by the same company in association with the nuclear engineering and reactor departments at Brookhaven together with the medical departments.

EXHIBIT 180. Detail of shutter mechanism and treatment port built in Brookhaven research reactor after completion of first series of treatments.



The conceptual design developed in some detail was received about 1 year ago and then was radically revised in a few features to provide an instrument which we now think a very appropriate one for this purpose (exhibits 181 and 182). The changes were not in the reactor itself to any large extent but were chiefly in placement of shielding and provision of shutters to increase operating efficiency for our own planned objectives.

EXHIBIT 181. Schematic cutaway to show some details of Brookhaven medical research reactor.



MEDICAL RESEARCH REACTOR

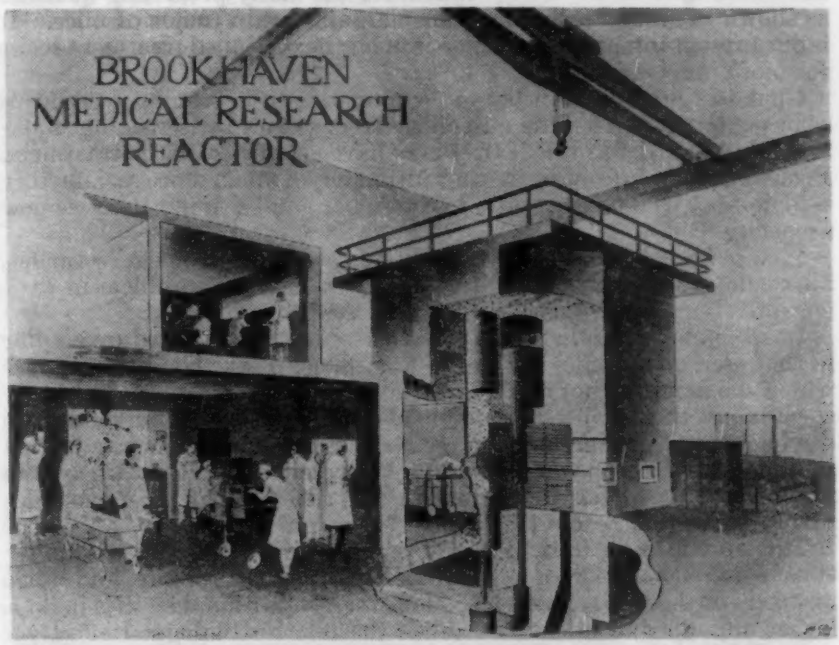
BROOKHAVEN NATIONAL LABORATORY

Within the very near future, a contract will be signed to construct this new medical reactor and we hope to take delivery approximately 18 months thereafter.

The new reactor will have many features of great value to us. It will permit exploration of the usefulness of epithermal or slightly more energetic neutrons as well as the thermal neutrons. Multiple studies can be carried out so that treatment and basic knowledge regarding neutron effects can be advanced simultaneously at a much more rapid rate than has been possible before.

The new reactor will also provide facilities for production of very short lived radioactive isotopes which we believe may prove useful in diagnosis and particularly in furthering our understanding of disease processes. It will have facilities for activation analysis of specimens taken from normal and diseased subjects. It will have facilities for the development of instrumentation of particular value to medicine in regard to radiation hazards of reactors and will also

EXHIBIT 182. Artist's conception of new Brookhaven medical research reactor in use during neutron capture therapy. Sections of reactor structure have been cut away to show component details.



permit radiation studies of animals as large as a goat which can be subjected to whole body radiation of varying types.

We have, by the design and construction of this instrument, capitalized on our present knowledge and experience gained in the neutron capture therapy program to develop a device having both special and general applicability within the fields of medicine and general biology. It is the result of many ideas suggested by the most competent nuclear engineers and meets our design requirements as clearly as we can define them in the present state of knowledge.

Although we believe the new reactor will satisfy our neutron flux requirements there are many other facets of the problem of neutron capture therapy which are also under research and development.

The problem of toxicity of the boron compound used for injection has received much study. Dr. Easterday has found that glucose in the proper amount decreases the toxicity of borax and it is this finding that enables us confidently approximately to double the boron dose for our second series of patients.

However, we must concern ourselves not only with the prime safety of the boron compound alone but also what effects concomitant drug treatment may have on boron pharmacology. Thus the interaction of boron compounds and morphine, demerol, promazine dilantin, and other drugs have been investigated that we may be aware of altered responses or the necessity for larger or smaller doses to achieve the effects desired under the actual conditions of treatment.

Dr. Easterday has also given extensive study to another inorganic boron compound, a pentaborate as contrasted with the tetraborate we have used until now. The pentaborate has many promising qualities as shown in animal tests of a transplantable brain tumor of mice. It is our present intention to include it in our next clinical treatment series for more precise evaluation.

Chemists interested in boron compounds are beginning to send us some compounds from the university laboratories for screening in our animal tests to determine if they may have usefulness in the treatment. Probabilities would indicate that ultimately a much more satisfactory vehicle for carrying the boron to the tumor can be found than we now are using.

We are happy about the growing interest in this problem in various university laboratories and hope that interest in this problem in various university laboratories will continue to grow.

In the experimental animal, we are now testing a procedure similar to that used on patients to determine empirically the conditions under which the mouse tumor can be killed. This datum accumulates slowly since many transplants must be made before all requisite conditions can be met but preliminary figures at 1 dosage value show a reduction in viability of the mouse tumor to 35 percent of that shown by the untreated tumor plus a doubling in survival time of the mouse implanted with the treated tumor.

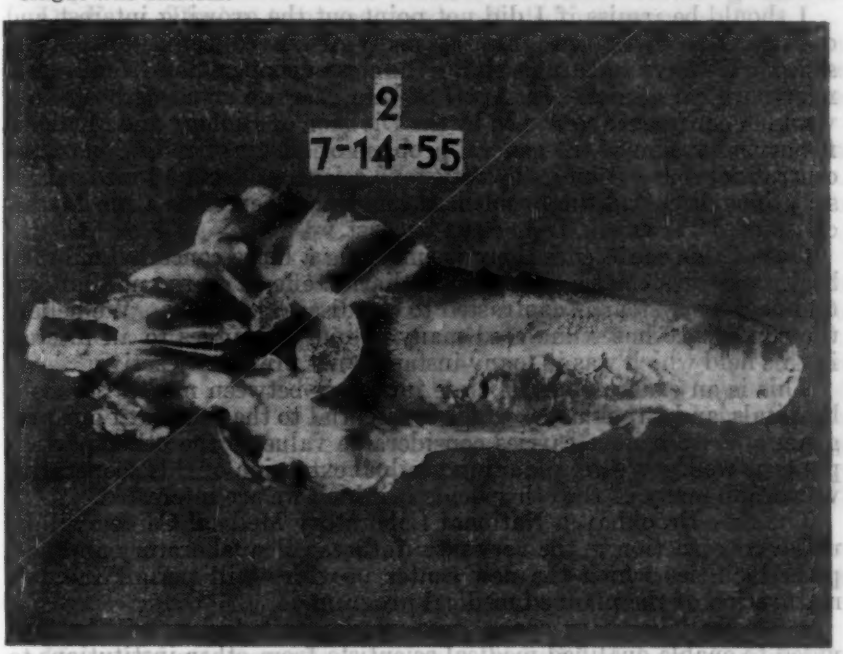
This, of course, is to help establish the dosimetry of this particular type of radiation. Dr. Bond, Dr. Robertson, Dr. Cronkite, and other members of the Department have done many additional studies in both larger animals and mice to establish the relative biological effectiveness—RBE—of capture radiation. Their data indicate that the RBE of the boron capture reaction is about 2.4 times that of equivalent gamma radiation.

The precise delimitation of effective action is shown in the tongue of a pig (exhibit 183) who had received a borax injection and subsequently was radiated with thermal neutrons. A very sharp line of demarcation was noted on the tongue of this animal between a region wherein the neutron flux was adequate and one in which it became inadequate because of decreasing numbers of neutrons. The line of demarcation between these two areas was of the same shape as predicted from tissue equivalent phantom studies of isodose neutron regions. It is clear evidence of the necessity for greater flux to achieve the desired depth treatment in our patients.

In discussing the safety of boron injections, I touched lightly on the development of new organic boron compounds which might be very much more efficient. In neutron capture therapy as with all treatment involving the use of radioactive isotopes, one of the major problems is so to control the movement of the therapeutic material within the body as to avoid extra hazards and to give maximum benefits.

The problem of placing boron at will in brain tumors is a special application of the general procedure. A large number of scientists in the medical department have been working on this general problem. Information of value has been obtained with studies with astatine 211 an alpha emitter of about 7 hours half life.

EXHIBIT 183. Tongue of pig after receiving boron and neutron radiation. Lower section of tongue is completely necrotic. Upper section shows no gross changes and no significant histological changes. This demonstrates dependence on flux for effective depth therapy. Boron distribution throughout tongue was uniform.



It is taken up in the thyroid gland like iodine but being an alpha emitter its effects would be similar on cells to the alpha particles resulting from thermal neutron capture by boron. The use of radioactive maganese-56 in palliation of liver malignancies, which Dr. Cotzias has under study, poses a problem in controlling distribution. The movement of sodium and potassium in nephrotic patients; the studies of electrolyte changes in hypertension and the fate of radioactive carbon-14 labeled amino acids, all have given information of value in obtaining a better understanding of the boron placement problem in our therapy.

We have concern with the mechanisms by which ions and molecules with and without charge penetrate cells, so the studies on cell permeability and distribution have yielded their dividends to the neutron capture program. The use of antibodies as a carrier to the tumor has been under investigation using other model systems for study.

The whole field of knowledge dealing with rates of distribution over short intervals is scanty and in general can be satisfactorily approached only by the use of radioactive isotopes. Some of the general principles governing distribution in mammalism systems, we believe we now are beginning dimly to perceive.

As these data can be obtained, oriented with respect to prior knowledge and interpreted, our capacity to localize an element or a compound almost at will within the body will increase. Such an increase

in our fundamental knowledge will permit a broad advance on all fronts wherein internally administered radioactive isotopes have value. All of the tools which atomic energy makes available to us are being used in these endeavors.

I should be remiss if I did not point out the growing interest and collaboration in this program by many of our colleagues in universities. We have and are receiving the closest cooperation from several neurosurgical clinics. In April of this year we acted as hosts to a working conference convened by the Division of Biology and Medicine for consideration of the general problem of effects of radiation on the central nervous system. Twenty-four scientists from 16 medical institutions discussed the problem at length. They came from Massachusetts to Texas, and from coast to coast.

Out of this conference there is emerging a large concerted effort to begin more systematic studies on radiation effects on the normal central nervous system as contrasted to the diseased regions. We believe the conference has stimulated many of our colleagues to an interest in this field which was in many instances not previously active.

This is an example of the close interplay between medical schools, hospitals, and Brookhaven which is essential to the success of our program and we believe carries considerable value to the other participants as well. We are planning gradual extension of this cooperative venture in many of the other fields in which we are interested.

The new Brookhaven National Laboratory Medical Center will be under construction in the very near future. The laboratory and hospital facilities which the new center provides will permit the full maturation of the planned medical program.

Adequate laboratory space, instruments, and devices will be provided to enable qualified medical scientists from other institutions to participate in the work at Brookhaven. Participation will be of two general kinds. In one, the visiting sicentists will engage with us in investigations which are inherently a part of the Brookhaven program and in the other they will utilize the special facilities at Brookhaven to accomplish investigations in their own programs which otherwise could not be carried out.

It is very stimulating to our staff to have these accomplished scientists with us, and, from statements of those who in the past have participated in such ventures, a similar stimulation is given to our visitors. We shall do our very best to keep it so.

Representative PRICE. For the time being, you are suspending neutron capture therapy pending the removal of some of the obstacles?

Dr. FARR. We have not suspended it because there are many problems that can be solved with the present reactor facility although it is recognized to be inadequate for definitive therapy. We can palliate the tumor effects and the results certainly show that palliation has been achieved. But the possibility of eliminating the tumor to the midline does not exist in our present situation.

Representative PATTERSON. Therefore the tumor is still alive?

Dr. FARR. The tumor is still alive in the deep region and it can extend to the other side and this is what has occurred uniformly in the patients that we have treated.

Representative PRICE. Are you continuing treatments now?

Dr. FARR. We are going to start a new treatment series this fall with our new boron compounds which may give us a somewhat further depth advantage than we now obtain.

Representative PRICE. When were the last treatments that you gave?

Dr. FARR. The last treatment was concluded in September 1955.

Representative PATTERSON. Could you not treat the tumor from both sides? That is, shoot it in from one side, Doctor, and then shoot it in from the other side and have them meet, which would cover the entire tumor?

Dr. FARR. When you consider the head as a sphere, one has within that sphere a smaller central sphere wherein neutron flux is inadequate. Therefore, no advantage can be gained by rotational exposures. With our new reactor, this limitation will be eliminated.

Representative PATTERSON. Does that only apply to the skull?

Dr. FARR. That applies to any region of the body. There will be the same neutron distribution in other tissues as has been shown to occur in the skull; it is not different from any other region of the body. Thermal neutrons are peculiar in this respect, in that while they do penetrate, they penetrate much as a gas does, without direction, and without velocity, but with a large decrease in numbers with depth penetration. Some of the neutrons decay themselves, others are captured by hydrogen, by sodium, and by other elements of the body which in the aggregate are very small in amount, because only a small region is covered.

Representative PATTERSON. Would there be any difference in the degree and size of the tumor itself, whether or not you can penetrate right through it? Are all of these tumors the same size?

Dr. FARR. No, sir; they are not.

If we had a tumor which lay only laterally, that one presumably we would be able to eliminate. We are hoping that we may be able to find a patient with exactly that kind of a situation. Now, one reason for continuing our present treatment is that we can do something for these people. We can palliate. We also can verify our measurements and our estimations of the effectiveness of our boron placement in the tumor by doing studies subsequent to autopsy, to firmly establish what neutron flux is necessary in order to eliminate the tumor.

In the patients who have been treated, we have never had tumor growth laterally. It has always been in the central region where our treatment was ineffective.

Representative PATTERSON. Have you had any patients who have been completely cured?

Dr. FARR. No, sir; we have not.

Representative PATTERSON. Regardless of the size of the tumor?

Dr. FARR. Regardless of the apparent size of the tumor at the time of operation. This is very characteristic of this particular tumor. This has been the one very discouraging experience of the surgeon. Frequently, upon operating he would find what would seem to be a very small tumor, which he thought he could surgically extirpate completely. He would do so only to find that there was a recurrence or apparent recurrence and the patient went on to death in about the same length of time as he would have if he had done nothing.

Representative PATTERSON. Could that be because there is some kind

of a seed in the blood and it would take it to other portions of the body?

Dr. FARR. This brain tumor does not grow in any region except the brain. It has not been conclusively established for this tumor whether there is a substance which arises within the tumor and modifies the surrounding region leading to further growth of the tumor or whether tumor development is inherent in the individual himself once the disease is manifest.

There is some evidence that the cells around the tumor are modified. They are not yet tumors, but one sees areas of swelling. In this instance, by this particular approach to the treatment, those cells that we might say were prelesional, as well as those frankly malignant would pick up boron because they will have an alteration in their qualitative reception of boron as compared with the normal cells. This biochemical cellular discrimination.

Representative PATTERSON. Are they eliminated?

Dr. FARR. They would be eliminated.

Representative PATTERSON. Permanently?

Dr. FARR. Yes, sir.

(Slide.)

Dr. FARR. You have seen pictures of treatments in the present facility to show you the rather cramped quarters, and the limited accessibility that we have to the present quarters.

Representative PRICE. Those things are being corrected?

Dr. FARR. Yes, sir. Let me show you some plans for the new reactor.

(Slide.)

Dr. FARR. This is the schematic diagram of the new reactor. The core of the reactor is in the center, and you can see it is surrounded by graphite with heavy watertanks which can be filled or empitied at will, permitting us to alter the energy of the neutrons which emerge, which will effectively enhance the depth dose.

The large shutters weigh about 21 tons and are made of heavy concrete. The treatment port to the treatment room can be enlarged up to 16 inches square. The shutters can be opened and closed within a matter of two seconds through active pressure hydraulic mechanisms which wil permit a very sharp differentiation of treatment.

(Slide.)

Dr. FARR. This is the artist's conception of what the new reactor will look like. It is partially cut away to show some of the components. Again, we have the core, the graphite reflector, the treatment cone, and the patient in the treatment room. The physician stands in the control area behind the shielding wall and observation windows to permit visual contact with the patient. In the new reactor with the lateral port, we have 180 degrees laterally within which we can manipulate the patient and we can approach the patient from either the vertical or the horizontal, so we will have great flexibility in accessibility for proper positions to bring the major number of neutrons to bear on the tumor which previously, of course, will have been explored by the surgeon, because this is necessary in order firmly to establish the diagnoses.

You see a number of people illustrated in this picture. Actually, each of these persons will have a necessary function to fulfill during

treatment and we eliminated some because there was not room to put them in and still have an informative drawing. With the new reactor some of the exposures may be as short as 2 minutes, as compared to our present 20 minutes. If you will remember that sharp peak of the curve, if we can hit 2 minutes on the top of that, we will very materially enhance the effectiveness of the treatment.

We think that with our new reactor as far as neutrons are concerned, we will have a facility which will give us flexibility, accessibility and the flux which this type of operation requres.

Representative PATTERSON. This is not only treatment for brain tumor but treatment for all tumors?

Dr. FARR. In principle, this is applicable to tumors lying deep within the body in all regions. I have been told that there is a group in at least one university that is working on some of the deeper tumors in the adbodminal cavity in the hope that they will be able to use this reactor to test out the efficiency of therapy in cases of that nature.

Representative PRICE. Does that conclude your statement?

Dr. FARR. That concludes my statement.

Representative PRICE. Doctor, in addition to your studies on tumors of the brain, what other major studies are you making at Brookhaven Laboratory?

Dr. FARR. Dr. Cronkite is making extensive studies on hemorrhagic diseases for two reasons. One is that these are important diseases in their own right, and second is the prevalence of hemorrhagic states following radiation exposures. This is a very difficult and serious problem and requires further elucidation.

Dr. Dahl is working on hypertension—high blood pressure. Sodium certainly plays some role though it may not be primary in the production and maintenance of hypertension. We are using radioactive isotopes to examine electrolytes in hypertensive patients in order to come to a better understanding of why the elimination of salt in the diet results in a lowering of blood pressure in many hypertensive individuals. If we could understand this mechanism we might be able to treat this disease very much more effectively.

Dr. Shreeve is concerned with the problems of diabetes and metabolism of glucose. Drs. Van Slyke, Sinex, Popenoe, Hankes, and Stoner are studying the production and formation of protein in the body as muscular protein, as enzymes, and as antibodies, the specific protein substances that react against invaders of bacterial or viral nature. We are also studying the tendonous structures of the body, because these apparently lose their elasticity with age. It is possible at least to reproduce this phenomenon with radiation. For by taking a kangaroo tail tendon and irradiating it, it loses its elasticity. We do not know whether we are mimicking a part of the aging process in this. It is an intriguing thought because of many studies which are going on today which have suggested a premature aging as one of the effects of radiation.

Dr. Cotzias is making some preliminary studies on patients with Parkinson's syndrome and is studying many enzyme systems in the body. Through radiation, it looks like we may have a means whereby we can determine the state of distribution of at least one important enzyme in tissues without having to alter the tissue in any manner.

Other types of analyses require that one take a piece of tissue, grind it up, and extract the enzyme. Then one sees whether it is a small molecule or large molecule or associated with other compounds.

However, some studies with radiation have suggested that one may be able to radiate the tissue while it is still in the intact animal and then by removing it and making the proper observations one can come to a knowledge as to what actual form it existed in while in the tissue prior to radiation.

So that we are, by an indirect means, peering within the living intact cell to observe its chemical structure. These are some of the types of studies that we are carrying on.

Representative PRICE. Thank you very much, Dr. Farr.

I think, Doctor, we had better take a recess until about 2:30 because I know Mr. Patterson has a luncheon appointment, and I have an appointment. I would not want to rush the presentation of the witnesses. The presentations have been so fine and valuable that I would not want to rush through any of them.

Would there be any inconveniences?

Dr. DUNHAM. I think that they can be here.

Representative PRICE. I think every presentation that has been made here has been very valuable and informative, and instructive, and I do not think any of them should be in any way spoiled by rushing through them.

Thank you very much, and I want to thank the witnesses who have appeared this morning.

The committee will stand in recess until 2:30 p. m.

(Thereupon, at 12:05 p. m., a recess was taken until 2:30 p. m., the same day.)

AFTER RECESS

Representative PRICE. The subcommittee will be in order.

Are you substituting this afternoon for Dr. Dunham?

Dr. ELY. Yes, sir. I am Dr. Ely, Thomas Ely. I am the Assistant Chief of the Medical Branch of the Division of Biology and Medicine of the Atomic Energy Commission.

Representative PRICE. Will you present the next witness?

Dr. ELY. Our first speaker this afternoon is Dr. Joseph F. Ross. He is professor of medicine, professor of radiology—radiobiology—and associate dean of the School of Medicine at the University of California at Los Angeles. The title of his talk is the Contribution of Atomic Energy to the Study of the Blood.

Representative PRICE. Dr. Ross, we appreciate your staying over to testify this afternoon. We were a little crowded for time this morning, but we didn't want to sacrifice any of this material that you want to present. Therefore, we carried you over until this afternoon, even though we are handicapped because of lack of members, because the House and Senate are in session.

STATEMENT OF DR. JOSEPH ROSS, PROFESSOR OF MEDICINE, PROFESSOR OF RADIOLOGY (RADIOBIOLOGY), AND ASSOCIATE DEAN, UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE, LOS ANGELES, CALIF.

Dr. Ross. It is a privilege, Mr. Chairman, to be able to discuss this subject with you this afternoon. There are two primary uses for atomic energy in the field of hemotology. One is the therapeutic application of radioisotopes to the treatment of certain blood diseases. The other is in the study of the fundamental mechanisms by which blood is made and destroyed, and how these mechanisms are changed in disease states.

It is the research application that I primarily wish to speak to you about this afternoon. The usual hemotologic studies, such as red blood-cell counts and hemoglobin determinations, tell a physician whether or not anemia is present, but they provide little information in regard to the processes which caused the anemia to develop. By employing radioisotopes as "tracers" to label the blood cells and their constituents, it is possible to determine the rates at which blood cells are being formed and destroyed, how long they live in the circulation, where they are formed in the body, and where they are destroyed. These studies can be carried on in normal or diseased human subjects with a minimal disturbance of normal body processes, and with little or no discomfort to the subject. Such studies have contributed greatly to an understanding of how and why certain types of anemia develop.

"LABELING" WITH RADIOACTIVE ISOTOPES AND THEIR USE AS "TRACERS"

The application of radioisotopes to hemotologic research depends, in most instances, upon a radioactive atom being incorporated into a molecule or cell, which because it contains this radioactive atom, can be detected or "traced" even though mixed with millions of nonlabeled molecules or cells. Exhibit 184 illustrates how we can use radioactive iron to label hemoglobin and red blood cells. In the normal individual, hemoglobin—which is the red colored protein of the blood—and erythrocytes are manufactured in the bone marrow. In ordinary circumstances, the marrow incorporates an atom of ordinary iron (Fe^{56}) into the fragment of the hemoglobin molecule represented in the left-upper diagram of figure 1. This molecule becomes a part of the red blood cell which is released into the blood stream. If we give an individual radioactive iron (Fe^{59}) his bone marrow will use atoms of radioactive iron for building hemoglobin as indicated in the right-upper diagram of exhibit 184. These radio-iron containing molecules of hemoglobin are incorporated into erythrocytes which are thus labeled and can be detected with Geiger-Mueller counters, or other radiation detecting equipment.

EXHIBIT 184. "Labeling" of the hemoglobin molecule and the erythrocyte with radioactive iron. Left side of figure: Under usual circumstances, the bone marrow incorporates atoms of ordinary nonradioactive iron (Fe^{56}) into the prosthetic groups of hemoglobin molecules, which are, in turn, incorporated into erythrocytes. Right side of figure: If radioactive iron (Fe^{59}) is administered to the subject, his bone marrow incorporates the radioactive atoms into the hemoglobin molecules and erythrocytes—which are then "labeled" with the radioactive atoms and can be detected among millions of nonlabeled ordinary erythrocytes.

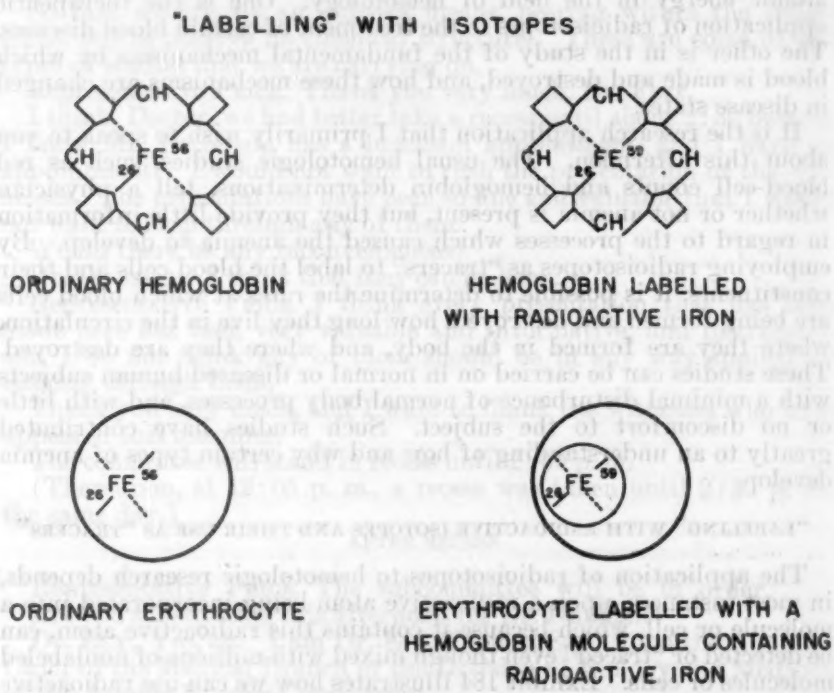


Exhibit 185 illustrates schematically the pathways followed by iron in the body. By injecting a small amount of radioactive iron into the blood stream, we "label" the plasma iron pool, and can measure the movement of iron into the bone marrow and red blood cells. Appropriate calculations based upon measurements of this iron turnover, and utilization indicate the rate of red blood cell formation. Exhibit 186 shows how injected radioactive iron is rapidly and almost completely incorporated into red cells by a normal subject. In contrast are the observations in patients with various types of anemia.

EXHIBIT 185. Metabolic pathways of iron in the body. Schematic representation of the pathways followed by iron in the normal human subject. The plasma iron pool occupies a central position since iron destined for various body tissues must pass through it. The amount of iron going to any particular tissue is roughly indicated by the size of the arrows. Quantitation of the amount of iron going to the bone marrow for synthesis of hemoglobin, and released into the blood stream in erythrocytes provides a measure of the rate of erythrocytes formation.

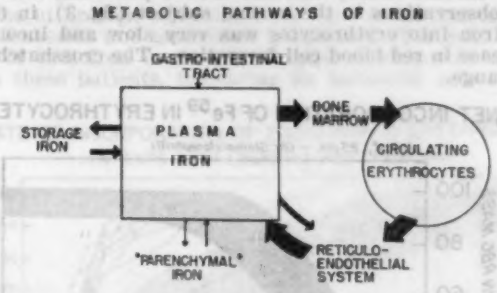
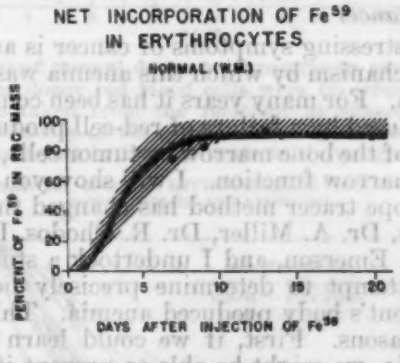


EXHIBIT 186. The utilization of radioactive iron for the formation of erythrocytes in a normal human subject. An injection of radioactive iron (Fe^{59}) was administered at "0" days. Samples of blood were removed at intervals and assayed for radioiron content. The radioactive iron was rapidly incorporated into the hemoglobin of erythrocytes formed in the bone marrow and was then released into the peripheral bloodstream. About 90 percent of the administered radioiron appeared in the circulating erythrocytes. The crosshatched area represents the normal range.



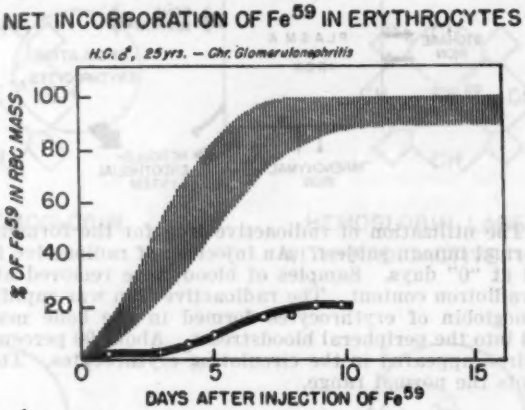
STUDIES OF THE MECHANISM OF ANEMIA

Kidney disease

In collaboration with Dr. M. Pollycove and Dr. L. Apt, we studied the utilization of radioiron and the rate of red-cell formation in patients with kidney disease. Exhibit 187 shows the results of such a study in a young man who had chronic kidney disease, uremic poisoning, and severe anemia. You can see that he built the iron into his red

cells very slowly and very incompletely. In other words, the anemia in this man was caused by the fact that, in addition to kidney failure, he had bone marrow failure, and was unable to properly manufacture blood cells.

EXHIBIT 187. Utilization of radioiron for the formation of erythrocytes in a patient with chronic kidney disease, uremic poisoning and anemia. In contrast to the observations in the normal subject (fig. 3), in this patient incorporation of iron into erythrocytes was very slow and incomplete, indicating marked decrease in red blood cell formation. The crosshatched area indicates the normal range.



The anemia of cancer

One of the distressing symptoms of cancer is anemia. Until fairly recently, the mechanism by which this anemia was produced was completely unknown. For many years it has been commonly believed that this anemia is caused by a failure of red-cell production brought about by replacement of the bone marrow by tumor cells, or by a hypothetical suppression of marrow function. I will show you how the application of the radioisotope tracer method has changed these beliefs.

My colleagues, Dr. A. Miller, Dr. R. Chodos, Dr. S. Finch, Dr. C. Crockett, Dr. C. Emerson, and I undertook a study of the anemia of cancer in an attempt to determine precisely how the presence of cancer in a patient's body produced anemia. This study was important for two reasons. First, if we could learn why these patients developed anemia, we might be able to prevent it or to treat it more effectively. Secondly, if we could ascertain why the presence of a neoplastic disease in the body of a human being makes him become anemic, we would gain important information as to the way cancer affects its host organism, information which might make possible more effective therapy of malignant disease.

Our studies were designed to determine three things: (1) How rapidly red blood cells were manufactured; (2) how long they lived in the circulation of the cancer patients; and (3) how rapidly they were destroyed. Radioactive iron was used to determine the rate and site of formation of the red blood cells in these patients, and radioactive chromium to determine how long they survived, and where they were destroyed.

Exhibit 188 shows the results of studies in a group of patients who had the cancerous condition of the blood known as leukemia or of the lymph glands known as lymphoma. The crosshatched area indi-

cates the normal pattern of iron uptake in normal subjects. In marked contrast, the patients who had cancer showed a more rapid than normal uptake of iron and an increased rate of red-cell formation. Although the normal person utilized half the injected radioiron for red-cell formation in 6 days, the patients with leukemia or lymphoma utilized half the iron in 2.7 days.

EXHIBIT 188. The utilization of radioiron for the formation of erythrocytes in patients with leukemia and malignant lymphoma. The rate of bone marrow incorporation of radioiron into newly formed erythrocytes was considerably accelerated in these patients, indicating an increased rate of red blood cell formation.

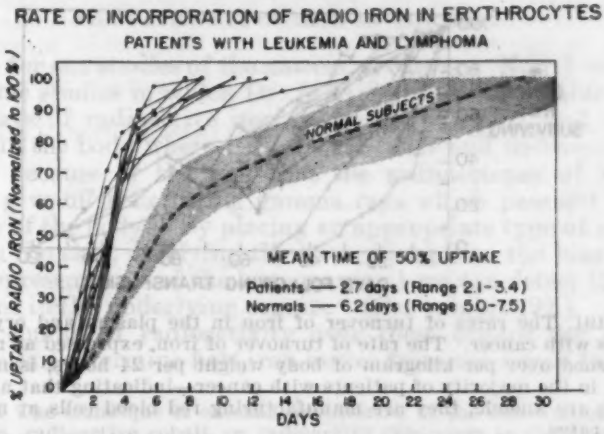

RATE OF INCORPORATION OF RADIO IRON IN ERYTHROCYTES
PATIENTS WITH LEUKEMIA AND LYMPHOMA
% UPTAKE RADIO IRON (Normalized to 100%)
NORMAL SUBJECTS
MEAN TIME OF 50% UPTAKE
Patients — 2.7 days (Range 2.1-3.4)
Normals — 6.2 days (Range 5.0-7.5)
DAYS

EXHIBIT 189. Survival of normal donor erythrocytes in patients with leukemia and lymphoma. The donor red blood cells were transfused at "0" days and blood samples were taken from the recipient at subsequent intervals and assayed for the persistence of the donor cells. The survival of the red blood cells was greatly shortened in these patients with malignant disease.

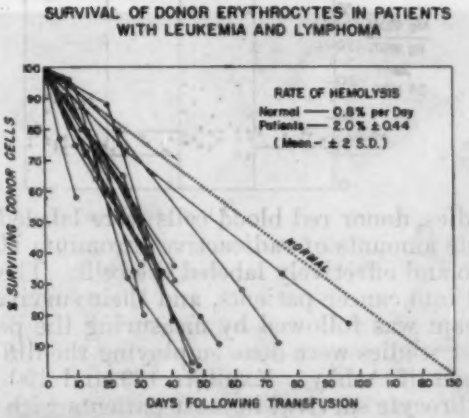


Exhibit 191 summarizes the rate of iron turnover in a group of patients with various types of neoplastic disease. In almost all of these patients the rate of iron utilization and red-cell formation was normal or increased. If patients with neoplastic disease are manufacturing blood cells at a normal or increased rate, why should they become anemic? If you manufacture blood twice as fast as a normal man, you should have twice as many red blood cells.

Exhibits 189 and 190 illustrate the reason why these patients became anemic. These figures depict studies of the survival of red blood cells in the circulating blood stream of cancer patients.

EXHIBIT 190. Survival of donor erythrocytes in patients with cancer. The majority of patients with cancer showed a decrease in the duration of survival of transfused erythrocytes. However, in some patients red-cell survival was normal.

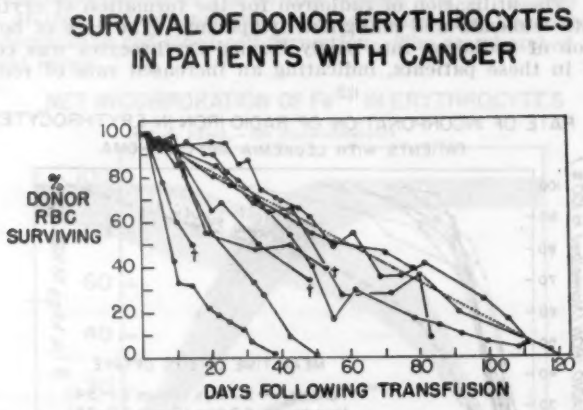
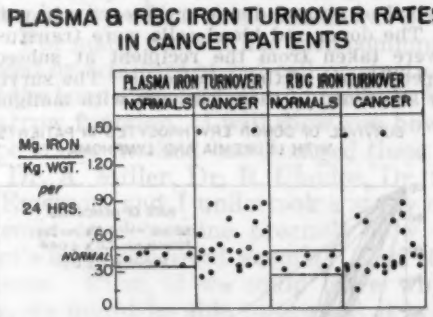


EXHIBIT 191. The rates of turnover of iron in the plasma and erythrocytes of patients with cancer. The rate of turnover of iron, expressed as milligrams of iron turned over per kilogram of body weight per 24 hours, is normal or increased in the majority of patients with cancer—indicating that although such patients are anemic, they are manufacturing red blood cells at normal or increased rates.



For these studies, donor red blood cells were labeled by incubating them with minute amounts of radioactive chromium (Cr^{51}) which became attached to and effectively labeled the cells. These labeled cells were transfused into cancer patients, and their survival in the recipients' blood stream was followed by measuring the persisting radioactivity. Similar studies were done employing the differential agglutinating technique of Ashby. Exhibits 189 and 190 show that the duration of erythrocyte survival in most patients with neoplastic disease is greatly shortened, in some instances being only 35 to 40 days, instead of the normal 120 days. As a reflection of this shortened survival, the rate of red-cell destruction is considerably increased. It is important to note that some patients did not have a shortened red-cell life span, and yet these patients, except for the absence of anemia, were indistinguishable clinically from those who did show marked shortening of red-cell life.

Thus, the cause of the anemia of cancer becomes plain—the survival of the red blood cells in most patients with cancer is greatly shortened, and although the bone marrow continues to manufacture red blood cells at a normal or increased rate, it does not compensate adequately for the increased demand for red cells. Thus, anemia develops.

These observations provide an excellent lead for further investigation. What is it that the cancer does to a man to shorten the survival of his red blood cells? Why should some patients clinically indistinguishable from the others, have no shortening of erythrocyte life span, and no anemia? More studies must be performed to answer these questions.

THE PATHWAYS OF IRON IN THE BODY

So much for our studies of the anemia of cancer. Now I would like to show some studies in which Dr. A. Miller and I were able to trace the pathways of radioactive iron in the body organs, and to detect the places in the body where red cells are made and destroyed. This is feasible because of the fact that the radioisotopes of iron and chromium give off penetrating gamma rays which pass out through the surface of the body. By placing an appropriate type of radiation detector on the skin, overlying the liver, the spleen, the heart, or the sacrum (representative of the bone marrow) we can detect the radioactive atoms in the underlying organs. (See exhibit 192.) By making serial counts of radioactivity over these organs for a period of days, we can determine how iron moves from one organ to another.

EXHIBIT 192. The technique of external monitoring of the distribution of radioactive iron, radioactive cobalt, or radioactive chromium in the organs of the body. A scintillation crystal radioactivity detector is placed at various sites overlying body organs (as indicated by the circles on the skin), and the gamma ray emissions from the radioisotopes in the underlying organs are detected and recorded by the scaling circuit. Serial measurements indicate changes in the amounts of the radioisotope in the various organs.

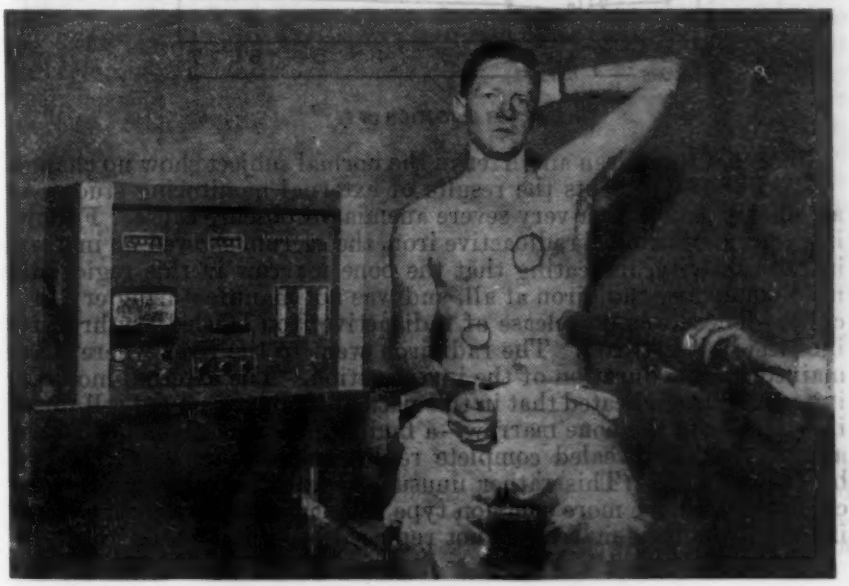
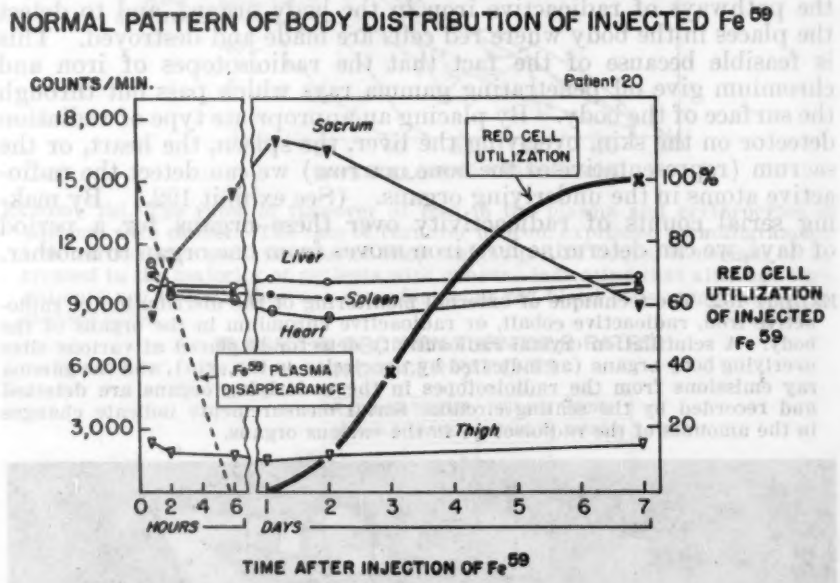


Exhibit 193 illustrates a series of such measuring in a normal subject. I call your attention to the measurements made over the sacrum, an area in which there is active red blood cell forming bone marrow. You will see how rapidly the radioiron is concentrated in this marrow and how after 24 hours a decrease in activity begins to occur. This decrease reflects the release from the marrow of newly formed radioiron containing red cells and is reflected by a progressive increase in radioiron labeled cells in the blood stream.

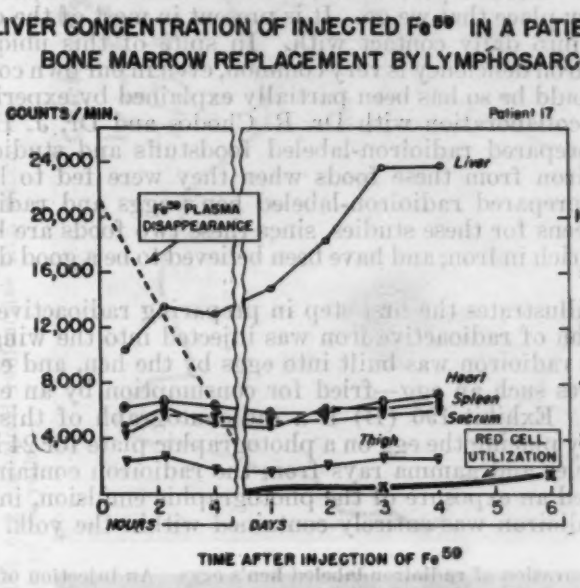
EXHIBIT 193. Pattern of distribution of injected radio iron (Fe^{59}) in the organs of a normal subject. Data secured by the method pictured in figure 9. There is rapid accumulation of the radioiron in the bone marrow (as represented by measurements over the sacrum) and rapid decrease in radioactivity of the marrow as the radioiron is released from the marrow in newly formed erythrocytes which appear in the circulating bloodstream (heavy solid line). There is no appreciable change in the radioiron content of the liver or spleen.



Note that the spleen and liver in the normal subject show no change.

Exhibit 194 presents the results of external monitoring studies in an elderly man with a very severe anemia, of obscure cause. Following administration of radioactive iron, the sacrum showed no increase in radioactivity, indicating that the bone marrow in this region did not take up any radioiron at all, and was not manufacturing erythrocytes. There was no release of radioactive iron labeled erythrocytes into the blood stream. The radioiron went to the liver where it remained for the duration of the investigation. The external monitoring procedure indicated that in this patient there was no red cell forming activity in the bone marrow—a finding subsequently confirmed at autopsy which revealed complete replacement of the bone marrow by tumor cells. (This rather unusual type of anemia must not be confused with the more common type of anemia previously discussed in which the bone marrow is not replaced by tumor tissue.)

EXHIBIT 194. Pattern of distribution of injected radioiron (Fe^{59}) in the organs of a patient in which the bone marrow had been destroyed by tumor (lymphosarcoma). In contrast to the normal pattern illustrated in figure 10, there is no accumulation of radioiron in the bone marrow of the sacrum, and practically no radioiron built into erythrocytes. Instead the radioiron is deposited in the liver, where it remains.



One of the problems that confronts doctors in regard to patients with anemia is whether or not an enlarged spleen is destroying blood cells more rapidly than it should, or whether it is actually manufacturing blood cells. The bone marrow in the normal individual is the site of blood formation, but if the bone marrow is destroyed by scar tissue or other disease, sometimes the spleen and the liver take over the function of manufacturing blood cells. However, we know that in certain conditions an enlarged spleen destroys blood more rapidly than normal. In some patients, our problem is to determine whether we had best take the spleen out or whether we should leave it alone.

Administration of radioactive iron to such a problem case followed by external monitoring over the spleen will usually indicate whether or not red cells are being made in this organ. Transfusion of radiochromium labeled red cells and external monitoring to ascertain whether or not radioactive chromium accumulates abnormally rapidly in the spleen will indicate whether or not the spleen is unduly active in destroying red cells. Simultaneous application of these two methods is possible, and has proved most helpful in indicating whether or not an enlarged spleen should be removed.

IRON DEFICIENCY ANEMIA AND THE ABSORPTION OF IRON FROM FOOD

Now, to turn to a different type of anemia. Anemia as you may know is one of the commonest afflictions of mankind. In the United States about 20 percent of all the patients who are admitted to general hospitals have anemia. In countries in which nutrition is not

as good as it is in the United States, the incidence of anemia is far higher. The majority of people who are anemic are so because their bodies are deficient in iron. They have iron-deficiency anemia. Why should this anemia be so common when iron is so very widely distributed in nature? About 5 percent of the earth's crust is iron, and iron literally is every place that we go. It is present in most of the objects that we come into daily contact with. In spite of this ubiquitous nature of iron, iron deficiency is very common, even in our own country.

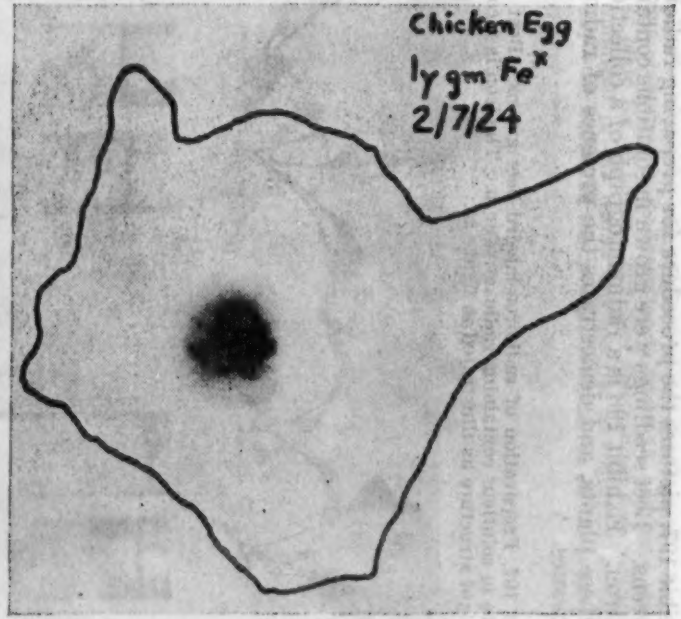
Why this should be so has been partially explained by experiments carried out in collaboration with Dr. R. Chodos and Dr. J. Halket, in which we prepared radioiron-labeled foodstuffs and studied the absorption of iron from these foods when they were fed to human subjects. We prepared radioiron-labeled hen's eggs and radioiron-labeled beet greens for these studies, since these two foods are known to be relatively rich in iron, and have been believed to be a good dietary source of iron.

Exhibit 195 illustrates the first step in preparing radioactive hen's eggs. A solution of radioactive iron was injected into the wing vein of a hen. This radioiron was built into eggs by the hen, and exhibit 196 (A) pictures such an egg—fried for consumption by an experimental subject. Exhibit 196 (B) is a radioautograph of this fried egg, prepared by placing the egg on a photographic plate for 24 hours. The beta particles and gamma rays from the radioiron contained in the egg produced an exposure of the photographic emulsion, indicating that the radioiron was entirely contained within the yolk.

EXHIBIT 195. Preparation of radioiron-labeled hen's eggs. An injection of radioiron solution is made into the wing vein of a hen.

EXHIBIT 196. (A) A fried egg laid by the hen pictured in figure 12, and (B) a radioautograph of the same egg. The egg contained radioactive iron which was concentrated in the central portion of the yolk.

A.



B.

82499°—56——18

Exhibit 197, pictures the procedure for preparing radioiron-labeled beet greens. Beet seedlings were grown in solutions containing radioactive iron. Exhibit 198 is a radioautograph of a collection of leaves from these plants, and demostrates the presence of radioiron in the plant tissues.

EXHIBIT 197. Preparation of radioiron-labeled beet greens. Beet seedlings are growin in solutions containing radioactive iron. The iron is incorporated into the plant structure as illustrated in figure 15.

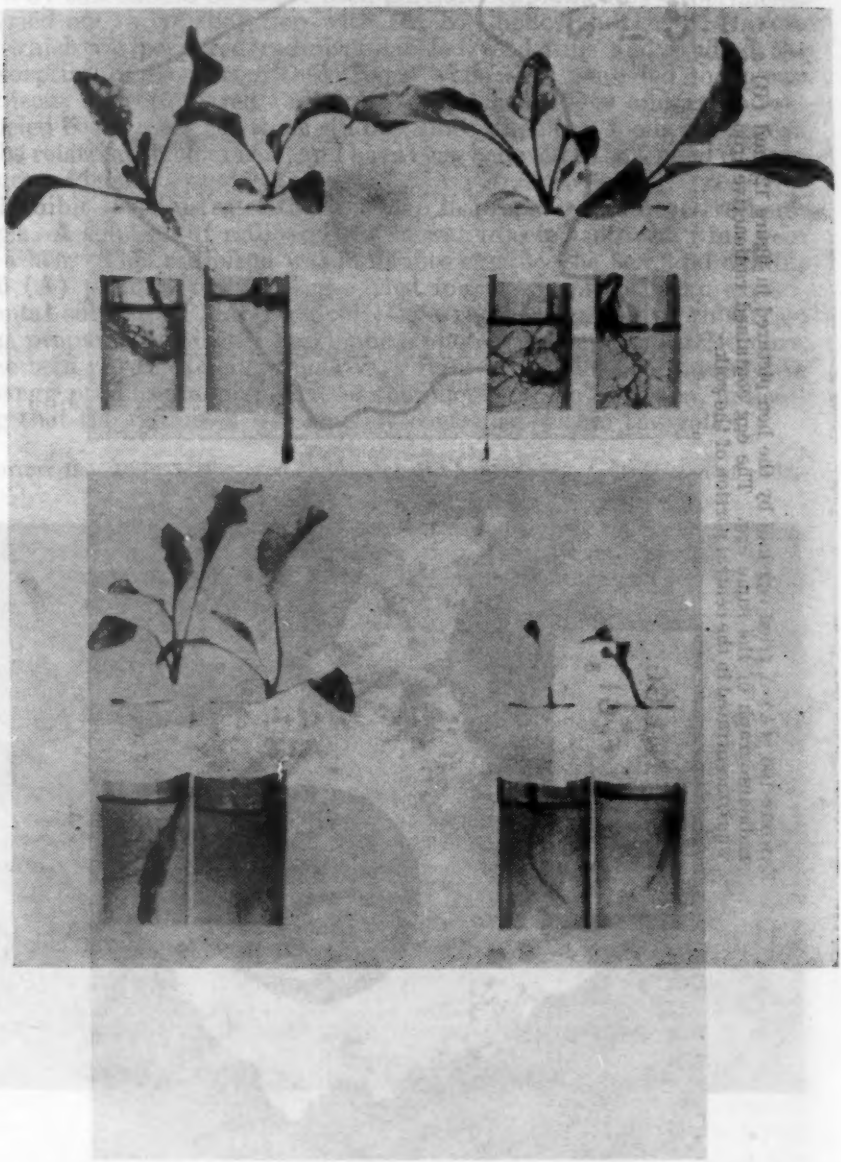
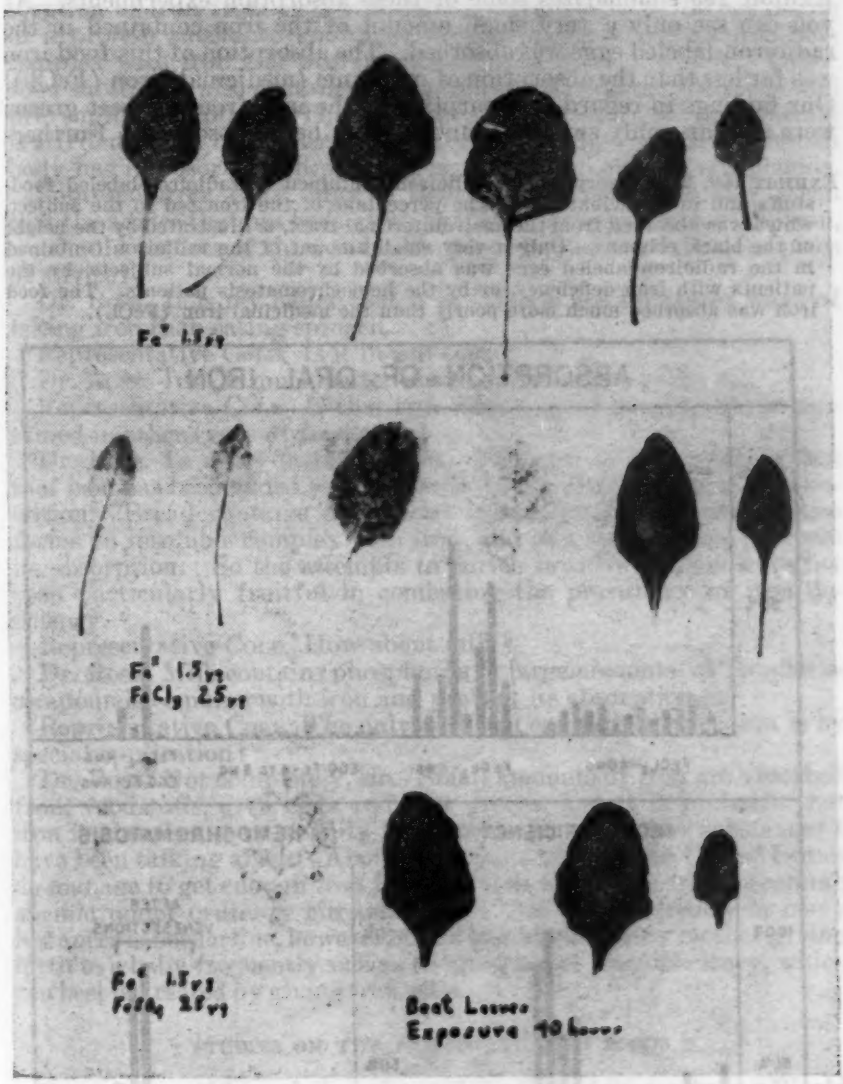
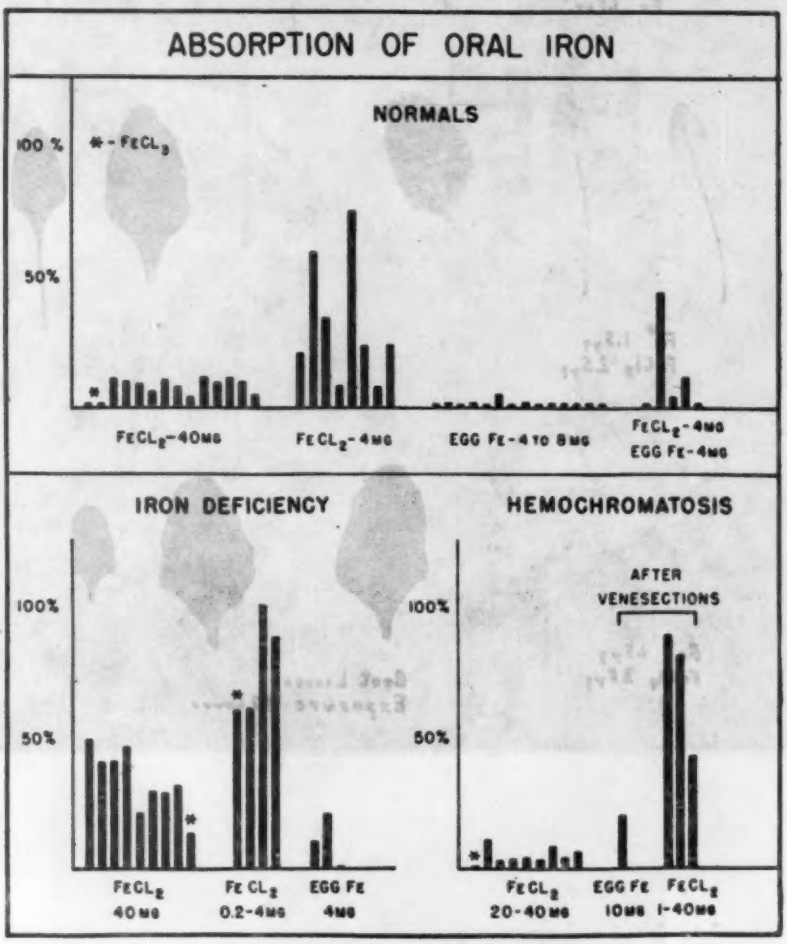


EXHIBIT 198. Radioautographs of radioiron-labeled beet leaves. Leaves were obtained from plants grown as illustrated in figure 14, and were placed on a photographic plate for 40 hours. The beta and gamma rays emitted by the radioiron contained in the leaves exposed the photographic emulsion; the density of exposure reflecting the amount of radioiron in the leaves.



These radioiron-labeled foods were fed to normal subjects and to patients with iron deficiency anemia and other condition. The amount of radioiron absorbed and utilized by the body, and the amount that passed through the gastrointestinal canal unused was measured. Exhibit 199 summarizes some of these absorption experiments. As you can see only a very small amount of the iron contained in the radioiron-labeled eggs was absorbed. The absorption of this food iron was far less than the absorption of inorganic (medicinal) iron ($FeCl_3$). Our findings in regard to absorption of the iron from the beet greens were similar—only small amounts of iron beign absorbed. Further-

EXHIBIT 199. The absorption of radioiron contained in radioiron-labeled foodstuffs and in medicinal iron. The percentage of the iron fed to the subject, which was absorbed from the gastrointestinal tract, is illustrated by the height of the black columns. Only a very small amount of the radioiron contained in the radioiron-labeled eggs was absorbed by the normal subjects, by the patients with iron deficiency, or by the hemochromatosis patients. The food iron was absorbed much more poorly than the medicinal iron ($FeCl_3$).



more, when ordinary eggs were fed to a subject simultaneously with inorganic iron, there was a marked decrease in the amount of inorganic iron absorbed.

Subsequent studies with Dr. T. Peters indicated that the poor absorption of iron from eggs was due to the presence in the egg white of a protein substance known as vitellin which forms an insoluble complex with iron and prevents its absorption by the body. Other food substances also contain compounds which combine with iron and prevent its absorption. Thus, the prevalence of iron deficiency anemia is attributable in large measure to the great difficulty which the human body has in absorbing these complex insoluble food-iron compounds.

Representative COLE. May I interrupt to ask: Does this mean that the advice that has been given us that because greens contain iron, we should eat lots of them to build up our bodies is a fallacious piece of advice?

Dr. Ross. It is my belief that it is. There are far better ways of taking iron than eating spinach.

Representative COLE. Is it in pill form?

Dr. Ross. Iron is much better absorbed from iron pills; yes.

Representative COLE. Is that true with respect to iron that is contained in other types of foodstuffs?

Dr. Ross. In many instances, yes. You may be aware of the fact that iron has been added to bread with the hope of improving iron nutrition. Bread contains a material known as phytate, which also forms an insoluble complex with iron, and to a large degree prevents its absorption. So the attempts to enrich bread with iron have not been particularly fruitful in combating the prevalance of iron deficiency.

Representative COLE. How about milk?

Dr. Ross. Milk contains phosphorus in large amounts. Phosphorus compounds combine with iron and prevent its absorption.

Representative COLE. The only way you can actually get iron is by special application?

Dr. Ross. Not completely, sir. Small amounts of iron are absorbed from foodstuffs, even eggs and beet greens, and it is probable that iron is absorbed more readily from meat than from the substances I have been talking about. About 80 percent of us in the United States do manage to get enough iron from our diet to keep us from becoming anemic under ordinary circumstances. Our iron nutrition in many instances is borderline, however, and a loss of blood, or a mother giving birth to a baby frequently suffices to bring about iron deficiency, which can best be treated by giving iron pills.

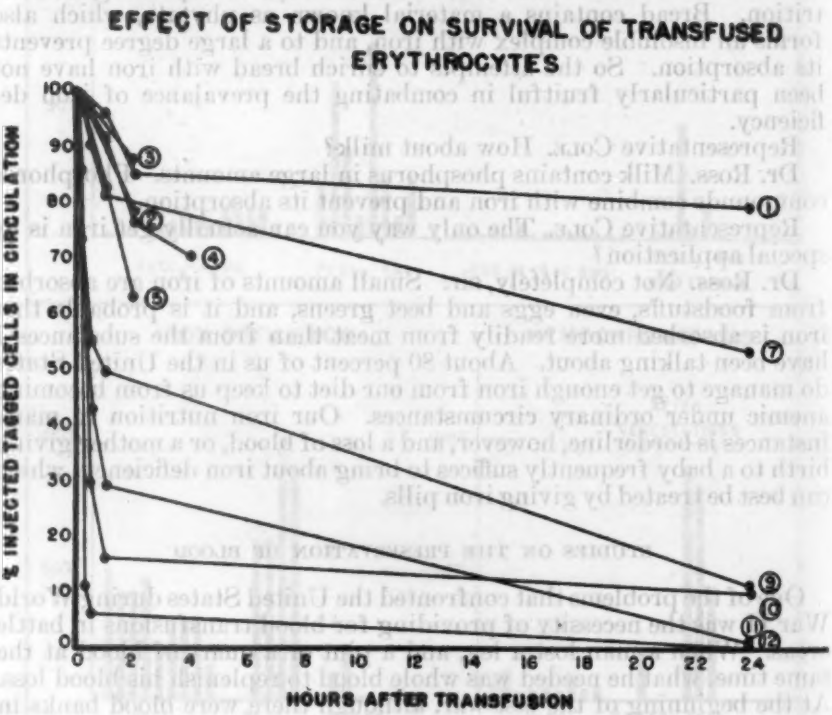
STUDIES ON THE PRESERVATION OF BLOOD

One of the problems that confronted the United States during World War II was the necessity of providing for blood transfusions in battle areas. When a man lost a leg, and a pint or a quart of blood at the same time, what he needed was whole blood to replenish his blood loss. At the beginning of the last war, although there were blood banks in this country, there was no good method available for preserving the red blood cells for a period of time long enough to allow their shipment to foreign battle areas. I wish to detail to you the way in which

radioactive isotopes were used to develop an effective method of preserving blood for shipment, a method which made possible provision of blood for transfusion purposes to every battle area where our troops were engaged.

A prospective blood donor was given an injection of radioactive iron and allowed to incorporate this into his red blood cells. He was then venesected and the blood stored in sodium citrate solution—the standard blood "preservative" before the studies described here. After various periods of storage, samples of this labeled blood were transfused into normal recipients. Samples of the recipient's blood were then taken at intervals for the next 24 hours and the amount of the radioactive iron-labeled stored blood still surviving in the recipient's circulation measured (exhibit 200).

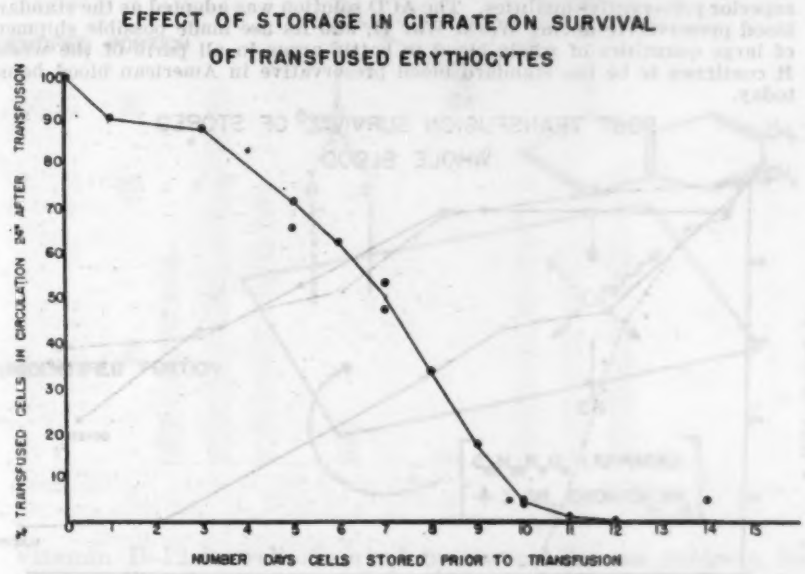
EXHIBIT 200. Evaluation of the effectiveness of sodium citrate as a preservative for red blood cells in blood stored in a blood bank. Blood was drawn from a donor who had been given radioiron. This blood contained radioiron labeled erythrocytes. Samples of this radioiron labeled blood were stored in sodium citrate solution at refrigerator temperature, and transfused into normal recipients after periods of storage ranging from 1 to 12 days. Samples of the recipient's blood were drawn at intervals after the transfusion, and analyzed for radioiron content. The disappearance of radio-active labeled cells from the blood stream of the recipient reflected removal of nonviable erythrocytes from the circulation. The number of transfused cells surviving 24 hours after transfusion indicated the effectiveness of the preservative.



As illustrated, sodium citrate was a very poor blood preservative. More than 30 percent of the cells stored for longer than 5 days were destroyed and disappeared rapidly from the recipient's circulation.

Using the survival of transfused cells 24 hours after the transfusion as a criterion of blood preservation, it is plain to see in exhibit 201 that sodium citrate is a very poor blood preservative. More than 30 percent of the cells stored for 5 days or longer did not survive.

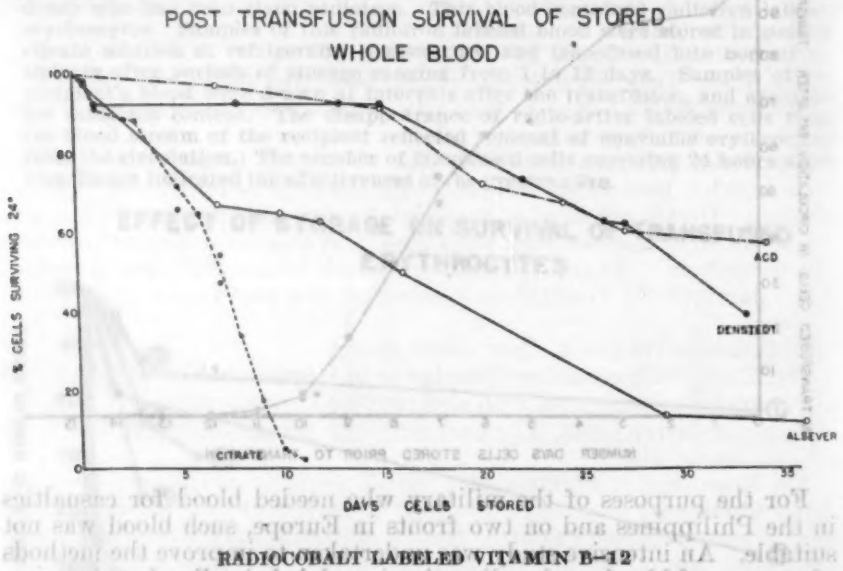
EXHIBIT 201. The effect of storage of whole blood in sodium citrate upon the survival of transfused erythrocytes: There is a progressive decrease in erythrocyte viability with prolongation of storage. After 5 days of storage less than 70 percent of the transfused cells survived for 24 hours after transfusion.



For the purposes of the military who needed blood for casualties in the Philippines and on two fronts in Europe, such blood was not suitable. An intensive study was undertaken to improve the methods of storage of blood, and radioactive iron labeled cells played an important part in the study.

Exhibit 202 illustrates the post transfusion survival of red blood cells stored in various preservative solutions. The ACD (acid-citrate-dextrose) solution was developed and was shown to be effective in preserving blood for a period of about 3 weeks—a period long enough to make possible air shipment to any battle area in the world. Hundreds of thousands of pints of blood preserved in this solution were flown overseas and transfused into our troops. In spite of many attempts to improve upon this ACD preservative, none have been successful, and it is still the standard for blood bank use.

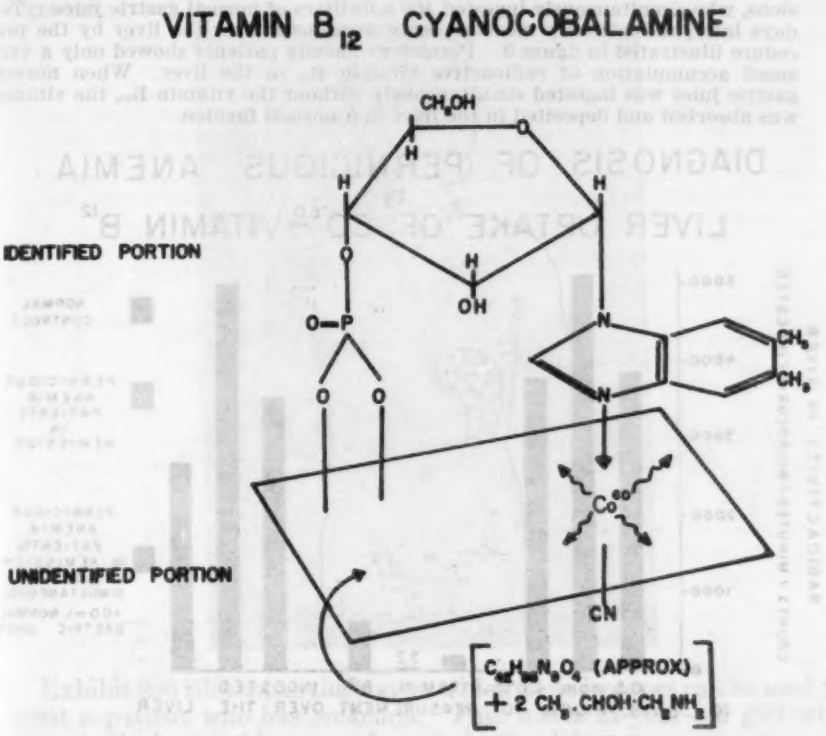
EXHIBIT 202. Comparison of various preservative solutions upon post transfusion survival of stored whole blood: The ACD and Denstedt solutions have superior preservative qualities. The ACD solution was adopted as the standard blood preservative during World War II, and its use made possible shipment of large quantities of whole blood to battle areas in all parts of the world. It continues to be the standard blood preservative in American blood banks today.



RADIOCOBALT LABELED VITAMIN B–12

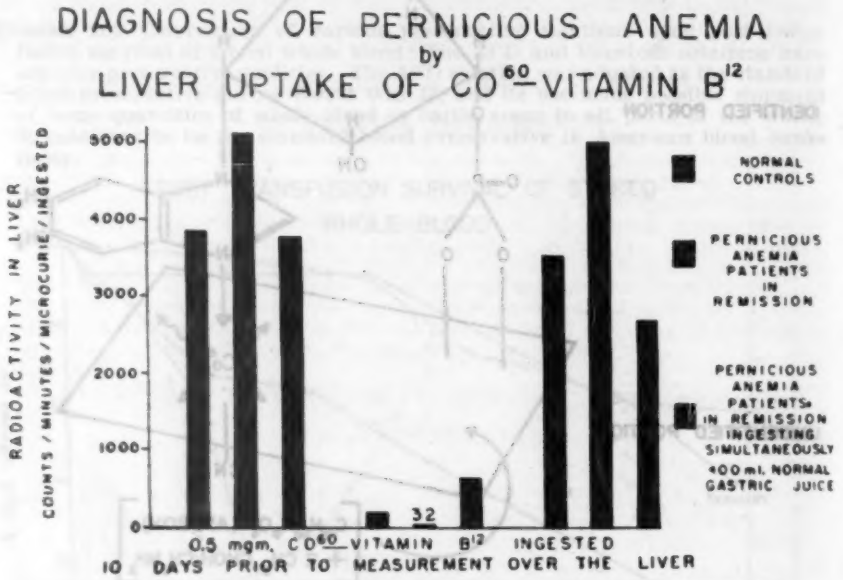
One of the very recent and quite interesting developments in hemotological research has been the discovery of vitamin B–12, and its preparation as a radiocobalt labeled tracer (exhibit 203). This vitamin is the specific agent for the treatment of pernicious anemia, and, also, has importance because of its requirement for human growth.

EXHIBIT 203. The structural formula of radiocobalt labeled vitamin B_{12} (cyanocobalamine). Radiocobalt (Co^{60}) is biosynthetically incorporated into the vitamin B_{12} molecule by fermentation of a medium containing tracer amounts of Co^{60} by Streptomyces griseus.



Vitamin B–12 is well absorbed by normal human subjects, but patients with pernicious anemia cannot absorb this vitamin unless another substance (known as intrinsic factor) which is contained in normal gastric juice is fed to the patient simultaneously with the vitamin B–12. These facts have made possible the development of a very simple and effective diagnostic test for pernicious anemia, as illustrated in exhibit 204. By feeding a minute amount of radiocobalt labeled vitamin B–12 and measuring the radioactivity appearing in the liver by external monitoring, it is possible to accurately diagnose pernicious anemia, even in patients who are in remission. This procedure has greatly improved the capacity of physicians to diagnose and provide good treatment to patients who have or have been thought to have pernicious anemia.

EXHIBIT 204. The diagnosis of pernicious anemia by evaluating the uptake of Co^{60} vitamin B_{12} by the liver: 0.5 microgram of cobalt 60 labeled vitamin B_{12} was fed to 3 normal controls (the 3 left-hand columns), to 3 pernicious anemia patients with therapeutically induced remissions (the 3 central columns), and to 3 pernicious anemia patients in therapeutically induced remissions, who simultaneously ingested 100 milliliters of normal gastric juice. Ten days later, radioactivity measurements were made over the liver by the procedure illustrated in figure 9. Pernicious anemia patients showed only a very small accumulation of radioactive vitamin B_{12} in the liver. When normal gastric juice was ingested simultaneously without the vitamin B_{12}, the vitamin was absorbed and deposited in the liver in a normal fashion.



THERAPEUTIC USE OF RADIOISOTOPES

Briefly, I wish to discuss the therapeutic application of radioisotopes in diseases of the blood. This subject was excellently detailed by Dr. John Lawrence before this committee 2 years ago. The most valuable radioisotopes for treatment of blood disease is radioactive phosphorus (P^{32}). It is effective and very useful in the treatment of leukemia and polycythemia vera. Exhibit 205 indicates schematically the fact that after an injection of radioactive phosphorus there is some localization of the radioactive atoms in the blood cells, lymph nodes, spleen and bone marrow. As these atoms undergo radioactive disintegration they release beta particles in these tissues and either destroy cells or inhibit their growth. It is this destructive and inhibitory effect that makes radioactive phosphorus a useful therapeutic agent in neoplastic and hyperplastic diseases.

EXHIBIT 205. The therapeutic use of radioactive phosphorus in leukemia and malignant lymphoma: Following injection radioactive phosphorus (indicated by the black dots) is deposited in increased concentration in leucocytes, lymph nodes, spleen, and bone marrow. Ionizing radiations (Beta rays) are released in these areas and destroy neoplastic cells with resultant inhibition of tumor growth.

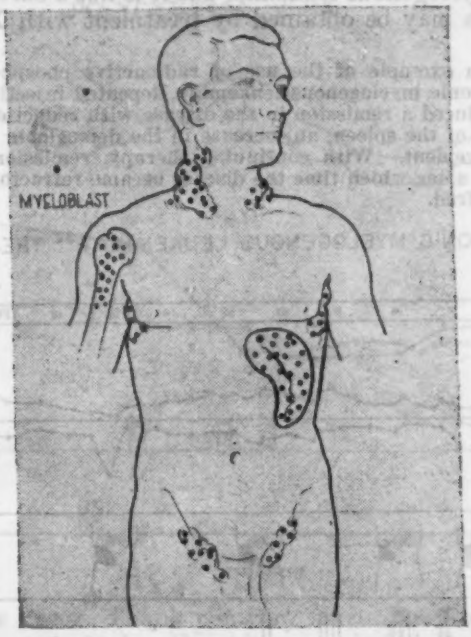


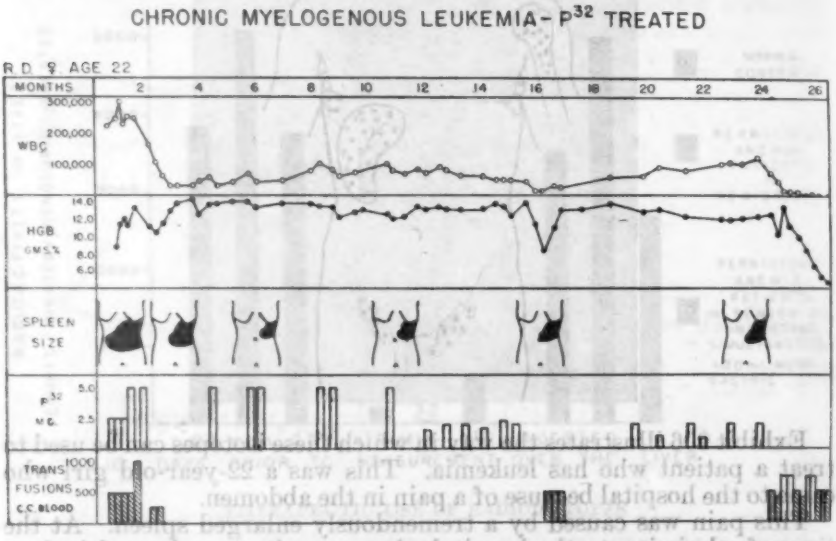
Exhibit 206 illustrates the way in which these isotopes can be used to treat a patient who has leukemia. This was a 22-year-old girl who came to the hospital because of a pain in the abdomen.

This pain was caused by a tremendously enlarged spleen. At the time of admission to the hospital, she was quite anemic, and had an extremely high white blood cell count. She was given radioactive phosphorus by intravenous injection, and this quite promptly reduced her white cell count to a normal level, and her anemia disappeared, and her spleen decreased in size. Then for an ensuing period of almost 2 years she was kept well and in a state of remission with repeated injections of radioactive phosphorus. The white count remained at normal levels. She was no longer anemic. She got married and filled a full time job.

At the conclusion of the 2-year period, the radioactive phosphorus was no longer effective. She became excessively anemic. Her spleen began to enlarge again, and she died. This is a typical example of the results achieved by treating myelogenous leukemia with radioactive

phosphorus. It is an effective treatment for a certain period of time. At the end of this period, usually 2 to 3½ years, treatment is no longer effective and in spite of the best possible management the disease relapses and the patient expires. Radioactive phosphorus is good therapy for myelogenous leukemia, but it is not a cure for the disease. Similar results may be obtained by treatment with X-ray.

EXHIBIT 206. An example of the use of radioactive phosphorus (P^{32}) in the therapy of chronic myelogenous leukemia: Repeated injections of radioactive phosphorus induced a remission in the disease with reduction in the leucocyte count and size of the spleen, an increase in the demoglobin level, and marked clinical improvement. With continuing therapy, remission was maintained for 24 months, after which time the disease became refractory to therapy, and the patient expired.



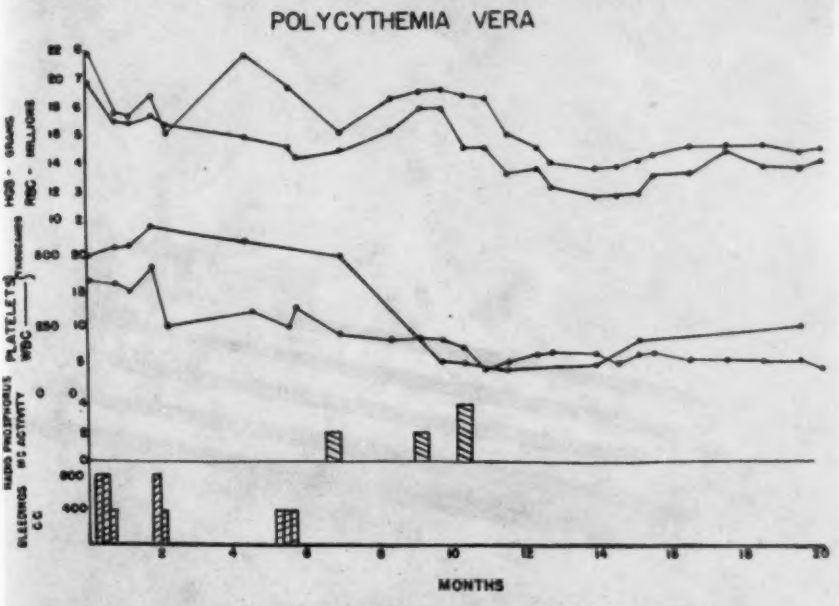
Another blood disease amenable to radiophosphorus therapy is polycythemia vera. Exhibit 207 illustrates a patient with this disease who had a red cell count of 6 million, which is about 1½ times normal. He was successfully treated with injections of radioactive phosphorus which restored his blood count to normal. The leucocyte count and platelet count also returned to normal and he continued in complete remission without the necessity for further therapy for 24 months.

In both of these disease states, radioactive phosphorus provides a very effective, convenient, and economical form of therapy.

SUMMARY

I have presented a few examples of the many and diverse contributions that research with radioactive isotopes has made to our knowledge of the physiology and pathology of the blood. Such studies have revolutionized our concepts of many aspects of diseases of the blood, and may be expected to lead to continued improvement in our ability to treat and to cure such diseases.

EXHIBIT 207. An example of the use of radioactive phosphorus in the therapy of polycythemia vera. Three injections of radioactive phosphorus induced a remission with reduction in the red blood cell count, hemoglobin level, leucocyte count, and platelet count. The remission persisted without further therapy for 24 months.



Representative PRICE. Thank you very much, Dr. Ross.

Dr. ELY. Our next speaker this afternoon is Dr. Paul V. Harper, who is associate professor in the department of surgery, Argonne Cancer Research Hospital in Chicago. Dr. Harper's talk is entitled, "Radioisotopes in Surgical Therapy."

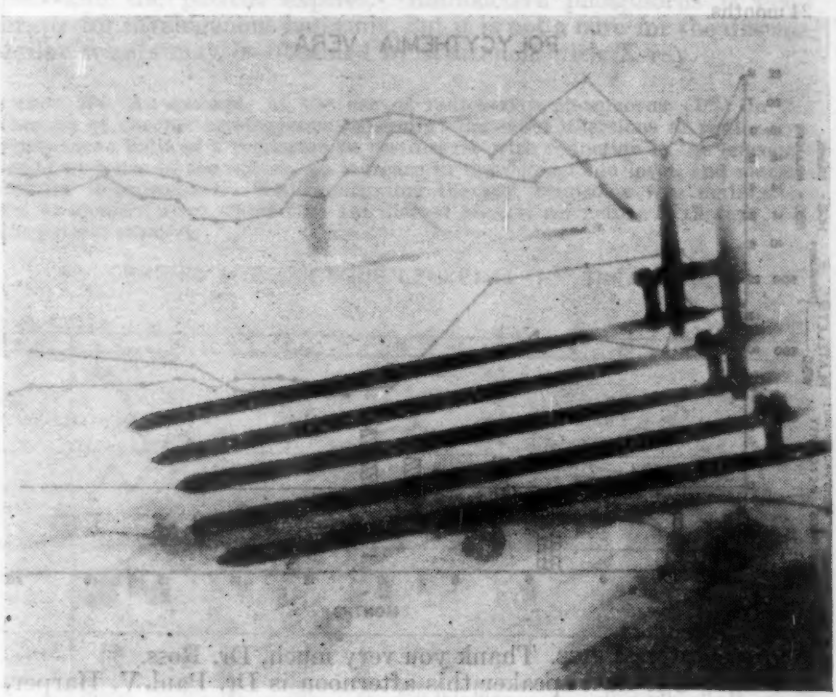
STATEMENT OF DR. PAUL V. HARPER, ASSOCIATE PROFESSOR, DEPARTMENT OF SURGERY, UNIVERSITY OF CHICAGO, IN THE ARGONNE CANCER RESEARCH HOSPITAL, CHICAGO, ILL.

Dr. HARPER. I wish to speak principally this afternoon about several projects which are being carried out at the Argonne Cancer Research Hospital. These involve the exploration of the possibilities of using various isotopes in connection with the surgical treatment of cancer.

To give some idea of the problems involved when one attempts to use radiation sources at operation I would like to show exhibit 208, a conventional radium implant in a tumor on the chest wall. The radium sources surrounding the tumor in this case are held in place by a special plastic device which keeps them spaced evenly in the proper geometrical placement to produce an even radiation field in the tumor. This is the aim of implant therapy. When a patient has a superficial tumor of this sort, it can be biopsied and the implant planned at leisure. The radium sources are prepared and when all is ready the procedure is carried out.

However, when one attempts to extend this type of treatment to a tumor inside the abdominal or chest cavity the situation is entirely

EXHIBIT 208. X-ray showing a radium implant in a tumor of the chest wall in which the radium needles are held in proper position by a special plastic holder in order to maintain the proper geometrical distribution of the radiation sources and produce thereby a uniform field of radiation in the implant.



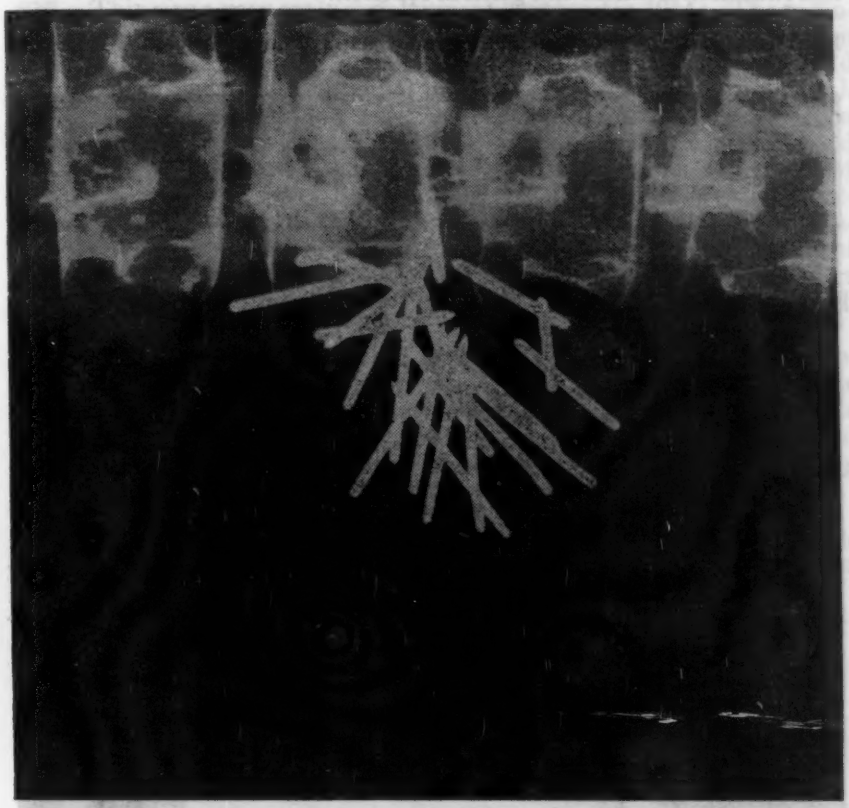
different. In the first place it is not known exactly what will be encountered when the abdomen is opened, or whether the situation will be favorable for an implant treatment. Nevertheless, if the possibility of an implant is contemplated it is necessary to have the radium needles or other radiation sources available.

The next slide shows an attempt at a free-hand radium implant (exhibit 209). Within the abdomen a form for holding the needles cannot be used. In this case the needles were placed individually by hand in what was thought to be a proper geometric pattern in a cancer of the pancreas. The random, irregular distribution which was achieved in spite of great care illustrates well the difficulties inherent in this procedure. These are aggravated by the fact that throughout the procedure there is a high level of radiation exposure for the surgeon who must handle the needles with long instruments and work with haste.

Representative PRICE. Are those the type of needles and instruments that Dr. Brucer told us about earlier?

Dr. HARPER. No; these are the conventional radium needles developed many years ago. They are sources of gamma radiation, and produce a uniform, quite localized cloud of radiation when properly implanted.

EXHIBIT 209. X-ray showing an intra-abdominal radium implant in a carcinoma of the pancreas in which the needles were put in singly by hand. The distribution and the resulting radiation field wah highly irregular.

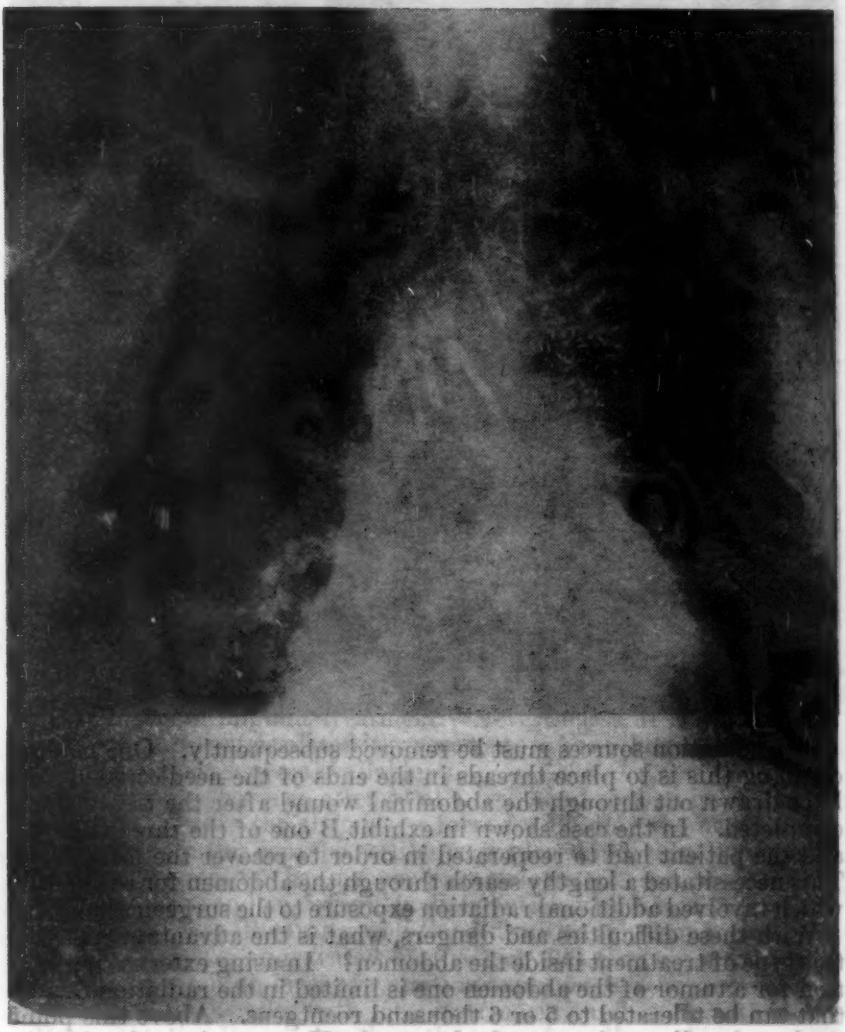


The radiation sources must be removed subsequently. One method of doing this is to place threads in the ends of the needles which are later drawn out through the abdominal wound after the treatment is completed. In the case shown in exhibit B one of the threads broke, and the patient had to reoperated in order to recover the lost needle. This necessitated a lengthy search through the abdomen for the needle, which involved additional radiation exposure to the surgeon's hands.

With these difficulties and dangers, what is the advantage of using this type of treatment inside the abdomen? In using external irradiation for a tumor of the abdomen one is limited in the radiation dosage that can be tolerated to 5 or 6 thousand roentgens. Above this point the bowel wall may be severely damaged. However, in an implant in which the radiation field is quite localized the bowel can be protected by transplanting it surgically away from the implant a distance of one-half to 1 inch and the radiation dosage can then be increased to 2 or 3 times what can be tolerated when using external irradiation. This is an area which has not been much explored in the treatment of intra-

abdominal tumors. In addition, because of the relatively much smaller volume of tissue radiated in an implant, the patient has much less radiation sickness and general reaction.

EXHIBIT 210. X-ray showing a large radon implant in an inoperable tumor of the lung.



A number of refinements have been developed, especially with the advent of isotopes, which enable us to overcome many of the difficulties which have been illustrated. One of the first is shown in exhibit 210. This was a very early development first used in 1914. The radioactive daughter element that gives most of the radiation from radium is actually a gas, radon, which can be trapped and sealed in little gold tubes called seeds, and implanted in the tumor. This is very helpful, because the radon decays with a half life of 3.8 days, and the radon seeds can be left in place permanently. In some large institutions and some veterans' hospitals, radon plants exist, so that radon sources of any desired strength are available if a situation is encountered unexpectedly where an implant is desirable. This is an exceptional situation. A radon plant is much too expensive an installation for most hospitals. When such a plant is not available it is necessary to order the radon whether it is actually used or not in order to have it on hand. Thus an unplanned procedure is in general impossible to carry out.

Exhibit 211 shows a device developed by the British in which radioactive gold grains are substituted for radon seeds. This is a gun-like device, discharging one gold grain from the tip of a graduated needle every time the trigger is pulled, thus permitting much more rapid and accurate placement of the radiation sources and in this way reducing greatly the exposure of the surgeon's hands to radiation.

EXHIBIT 211. A gunlike device for discharging radioactive gold pellets. This device makes it possible to make an implant much more rapidly and accurately than it is possible with the ordinary methods of introducing radon seeds.

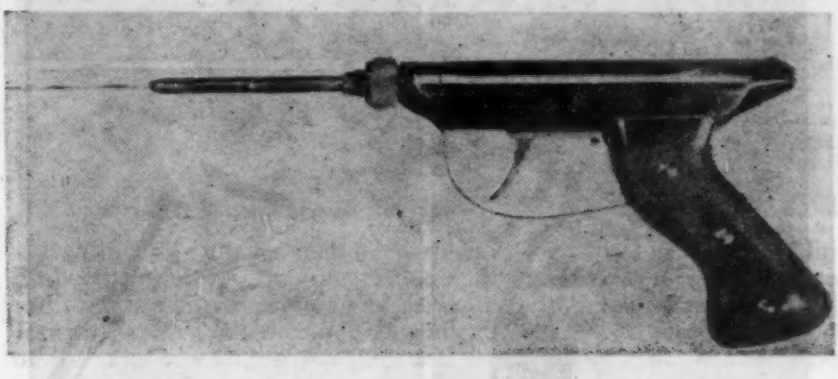
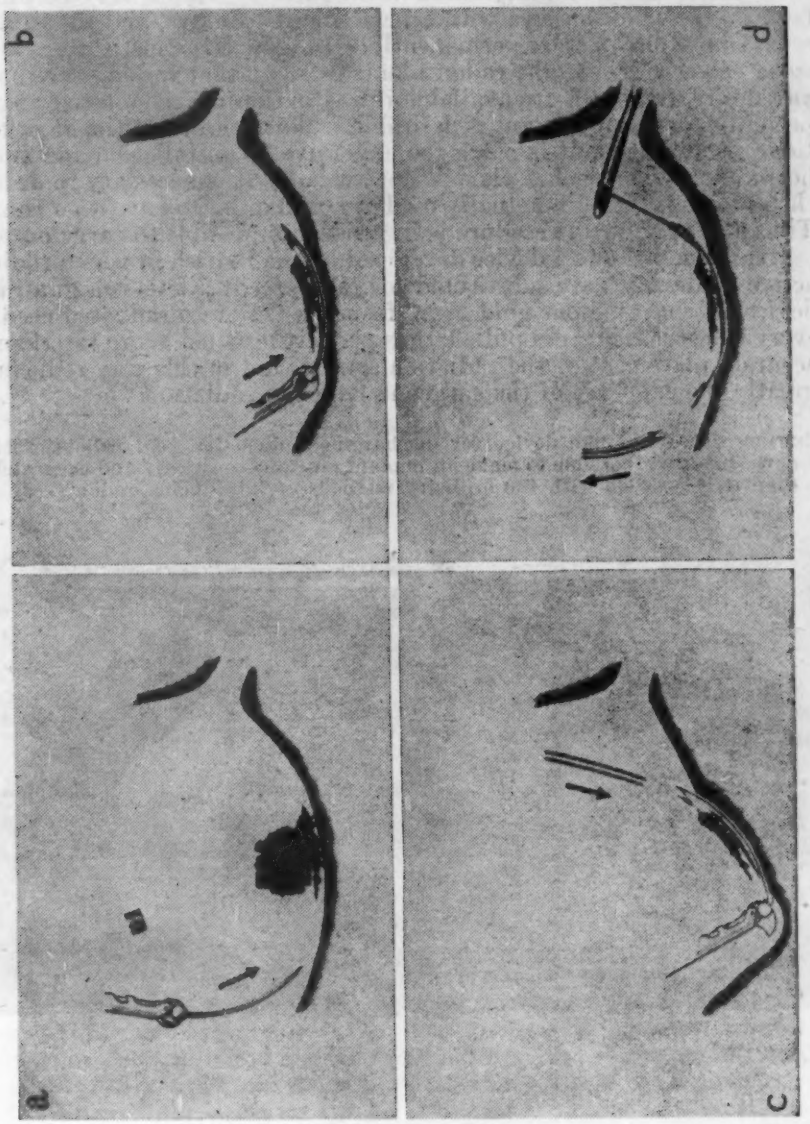


Exhibit 212 shows a method that has been devised by the British for circumventing another problem. In the case of a bladder tumor the patient is subjected to surgery, the tumor is removed, and then a

EXHIBIT 212. The placement of hairpin shaped radioactive tantalum wires in the base of a tumor of the bladder at surgery. These wires are subsequently withdrawn through the urethra following the completion of the treatment.



hairpin-shaped wire of long-lived radioactive tantalum is placed through the base of the tumor, and a thread attached to the bend of the wire is led out through the opening of the bladder. After completion of the treatment the radioactive wire can be withdrawn without reoperating on the patient. This has worked out quite satisfactorily. Exhibit 213 shows an X-ray of two of these hairpinlike devices in place.

EXHIBIT 213. X-ray showing two radioactive tantalum wires in place in a tumor of the bladder.

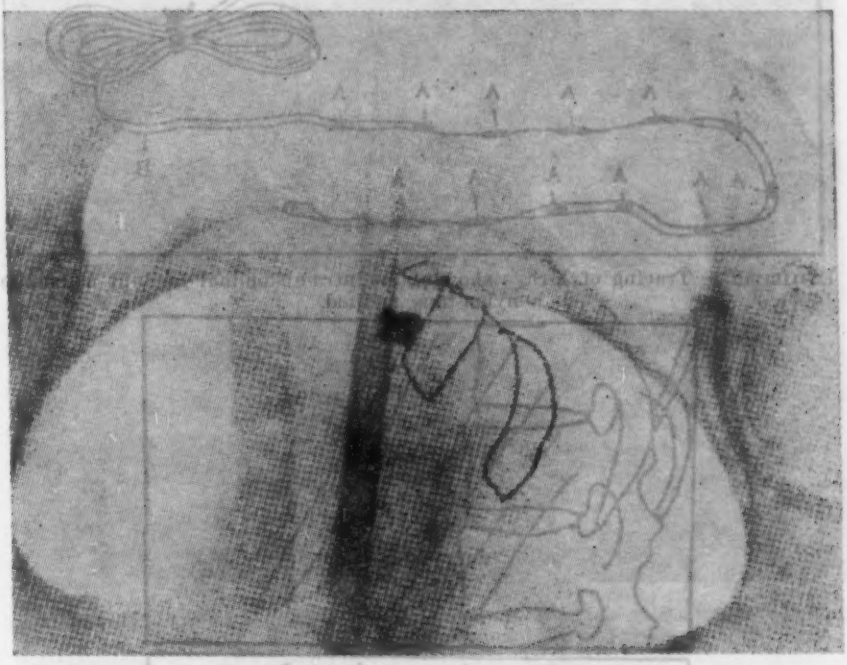


Exhibit 214 shows a method worked out by Dr. Henschke at Ohio State University. He constructed nylon tapes in which he placed radioactive sources, using a number of different radioactive materials: Radium, radon, cobalt^{60}, gold^{198}, and iridium^{192}. At surgery, the end of the tape containing the radioactive sources is kept in a lead box and the inactive leader is passed through the tumor. A number of these tapes are placed through the tumor and then, just before the end of the operation, the radioactive sources are rapidly drawn into the tumor. Following the treatment the tapes are withdrawn along with the sources. This works very well in reducing the radiation exposure of the surgeon and permitting a careful placement of the implant. Exhibit 215 shows a tracing from an X-ray showing one of these implants in the abdominal cavity.

We have attempted to devise a method which avoids completely the utilization of isotopes in the operating room, and hence removes all necessity for exposure of the operator, and of haste in the surgical procedure.

EXHIBIT 214. A nylon tape containing radioactive sources. A number of these are passed through a tumor using the inactive leader. When all the tapes are in place then the radioactive ends are drawn into the tumor rapidly. This permits careful placement of the implant without exposure to the operator.

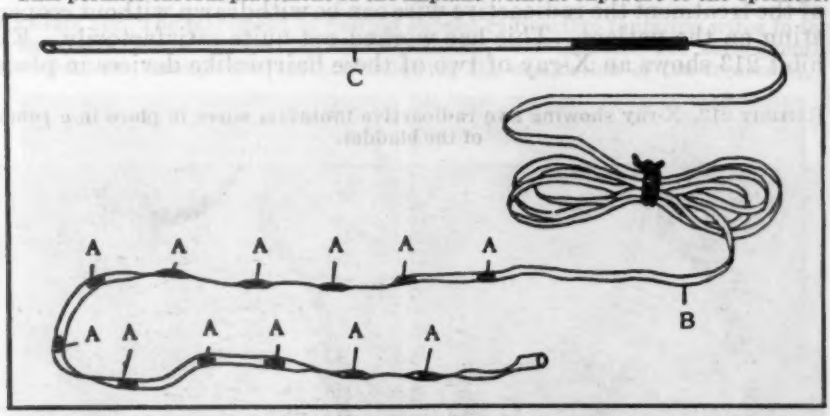


EXHIBIT 215. Tracing of X-rays showing an intra-abdominal implant using the nylon-tape method.

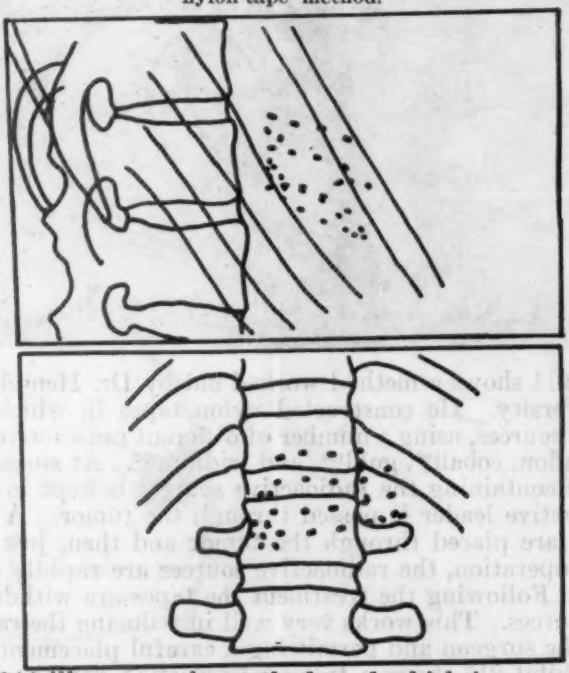


Exhibit 216 illustrates the method used which is a very fine polyethylene tubing no thicker than a surgical suture. This is sewed around and through the tumor following the Manchester distribution rules as closely as possible. The abdomen is then closed and both ends of the tubing are brought out through the wound. Subsequently, after the patient has recovered from the operation, radioactive isotope solution is drawn into the tubing (exhibit 217). There is no need for the operator to be exposed at any time during the procedure. The placement of isotope solution in the tubing takes about a minute, and involves very little exposure to radiation.

EXHIBIT 216. Very fine plastic tubing (Clay Adams PE/10) with an inner diameter 0.28 millimeter, an outer diameter 0.61 millimeter, used in making volume implants.

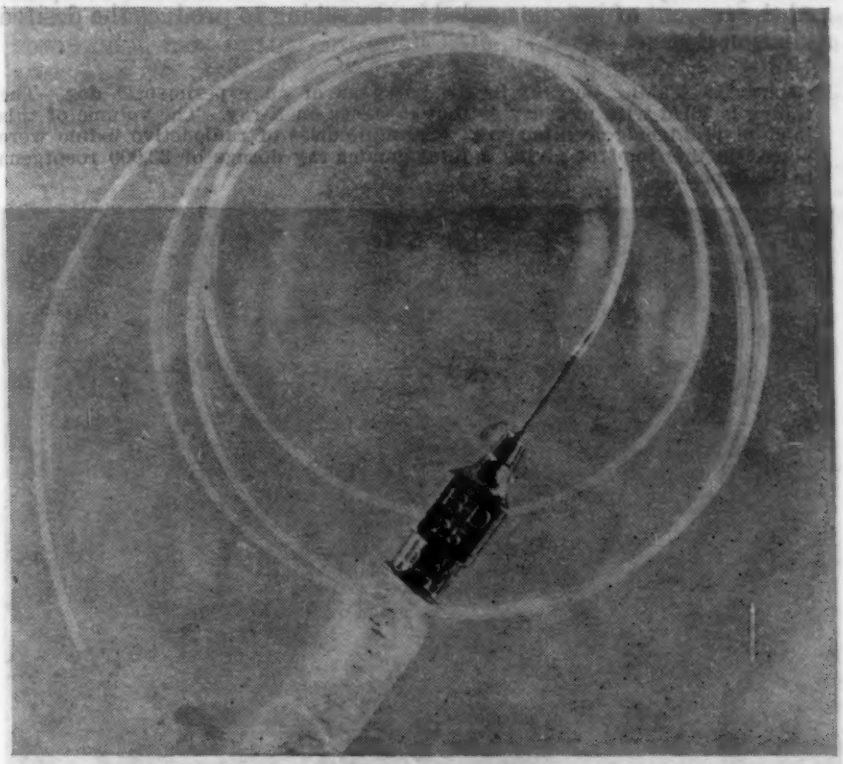


EXHIBIT 217. Diagram showing how isotope in solution is drawn into tubing implant.

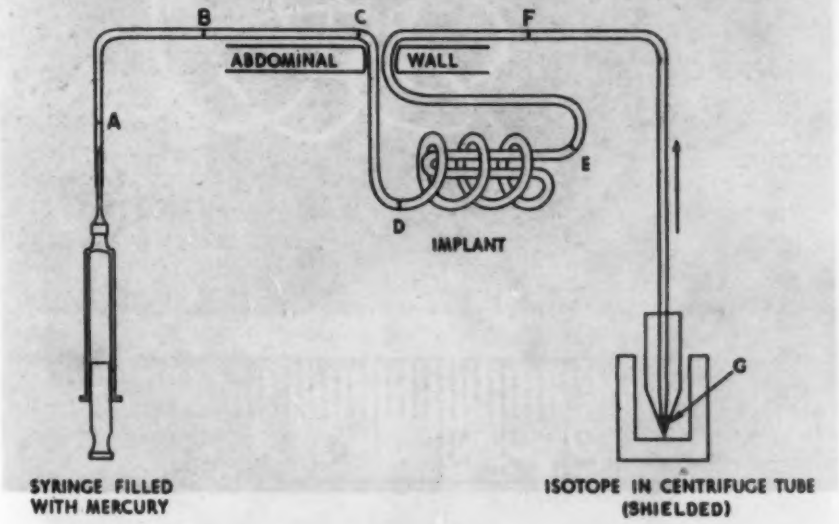


Exhibit 218 shows one of these implants in the pancreas of a dog. The tubing has been filled with mercury so it is visible by X-ray. In this way it is possible to calculate the volume of tissue in the implant and the amount of isotope needed in the tubing to produce the desired radiation dosage.

EXHIBIT 218. Tubing implant in the pancreas of an experimental dog. The tubing is filled with mercury so that it shows on X-ray. The volume of this implant is 3.1 cubic centimeters. 32.2 millicuries of radioactive iodine were placed in this implant giving a total gamma-ray dosage of 33,000 roentgens in the implant.

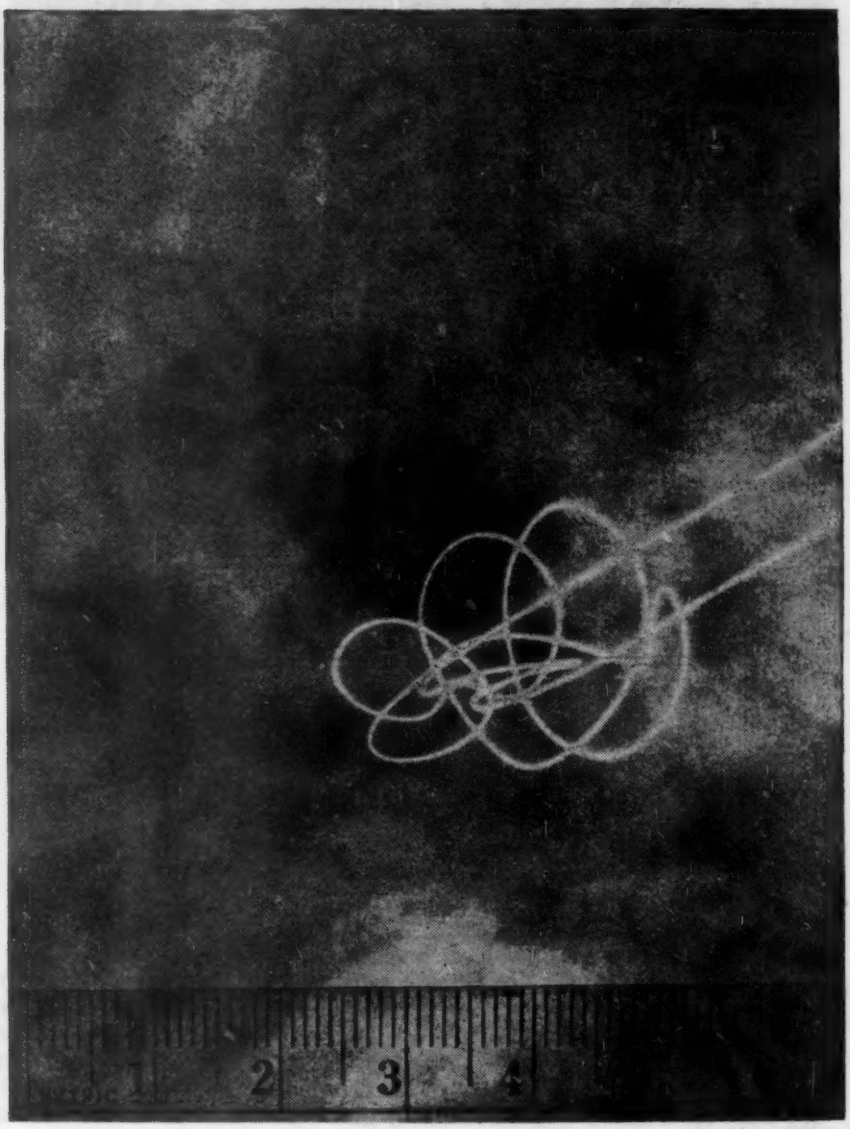


Exhibit 219 shows the region of the same implant 3 months later. In this experiment it was attempted to see how far the radiation dosage could be pushed. The animal was given 30,000 roentgens in the implant, many times what would ordinarily be given to a patient. The bowel lying next to the implant is undamaged as is the nearby pancreas and the portion of the pancreas in the implant is completely converted to scar tissue. The animal apparently experienced no significant ill effect from the procedure.

EXHIBIT 219. Microphotograph (×10) of the implant shown in exhibit 218. The nearby bowel is undamaged, the pancreas in the implant is completely converted to scar tissue in which can be seen ghosts of some of the acinar cells. The near pancreas is little damaged.

Exhibit 220 shows an implant in a patient in a cancer of the head of the pancreas. This type of tumor was chosen for this experimental treatment because it is, for practical purposes, incurable by surgery. The core of the implant is a little askew, because there is

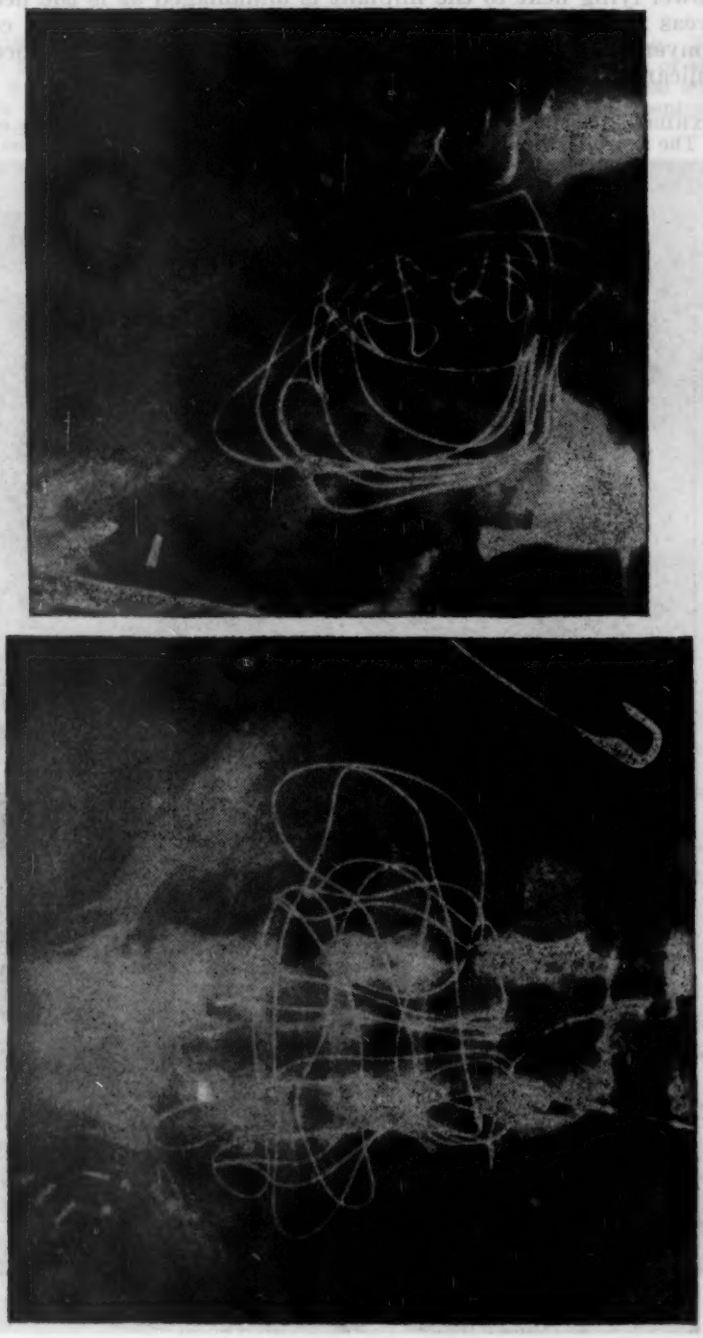


EXHIBIT 220. Anterior-posterior and internal X-rays of an implant in the head of the pancreas of a patient. This implant contained 121 cubic centimeters of tissue and 89.5 millicuries of radioactive iodine introduced into the tubing gave a radiation dosage of 9,470 roentgens.

a large blood vessel, the portal vein, running through it. We have treated 12 patients in this way with radiation dosages of 8,000 to 12,000 roentgens with almost no difficulty from general radiation reaction and in many cases with satisfactory palliation. The tubing, which remains permanently, causes no trouble.

Exhibit 221 shows a different type of device embodying the same principles. This consists of an envelope of polyethylene sheeting with a fine polyethylene tube leading to it. The envelope contains a sheet of blotting paper. This applicator is placed inside the patient against the region of the desired treatment, and after the patient has recovered from the operation the isotope in solution is introduced through the tube and soaks evenly through the blotting paper, thus spreading out the radiation source in a uniform plane.

EXHIBIT 221. A plane polyethylene applicator consisting of a piece of blotting paper in a polyethylene envelope to which fine polyethylene tubing leads for subsequent introduction of isotope solution.

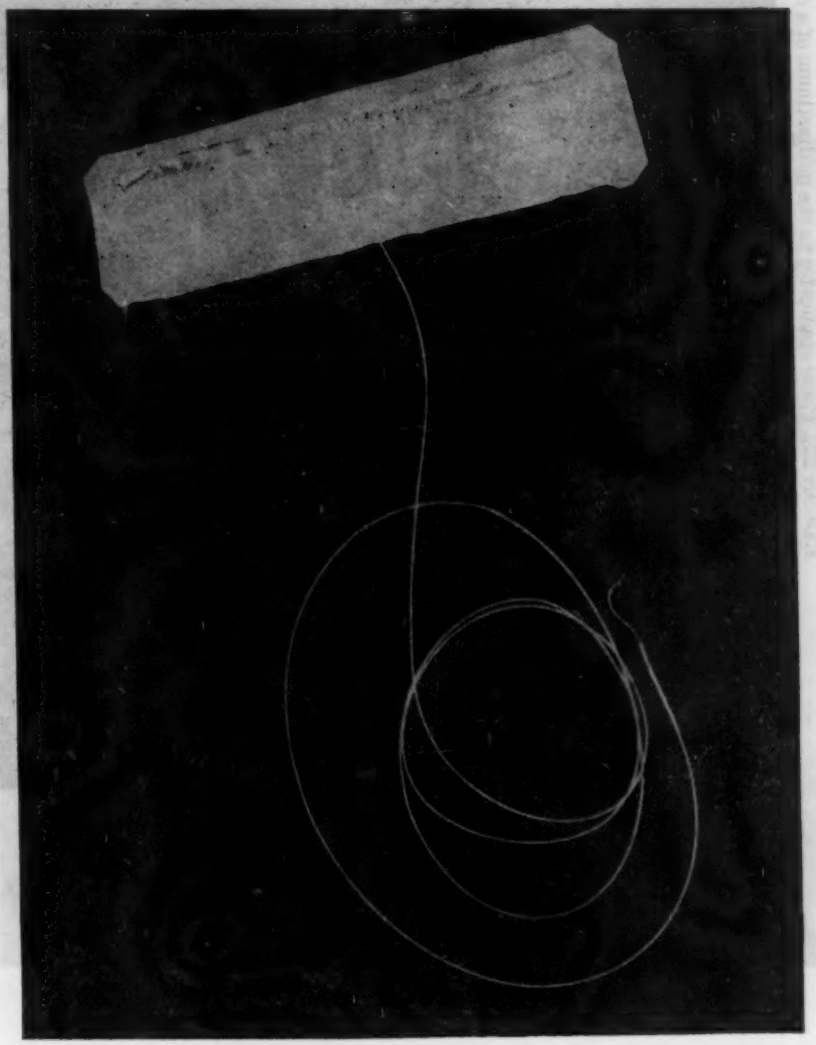


Exhibit 222 shows an experimental animal with such an implant in the chest. It is contemplated that this form of treatment would be ideal for very high level radiation of the internal mammary nodes in cases of carcinoma of the breast situated on the medial aspect of the gland.

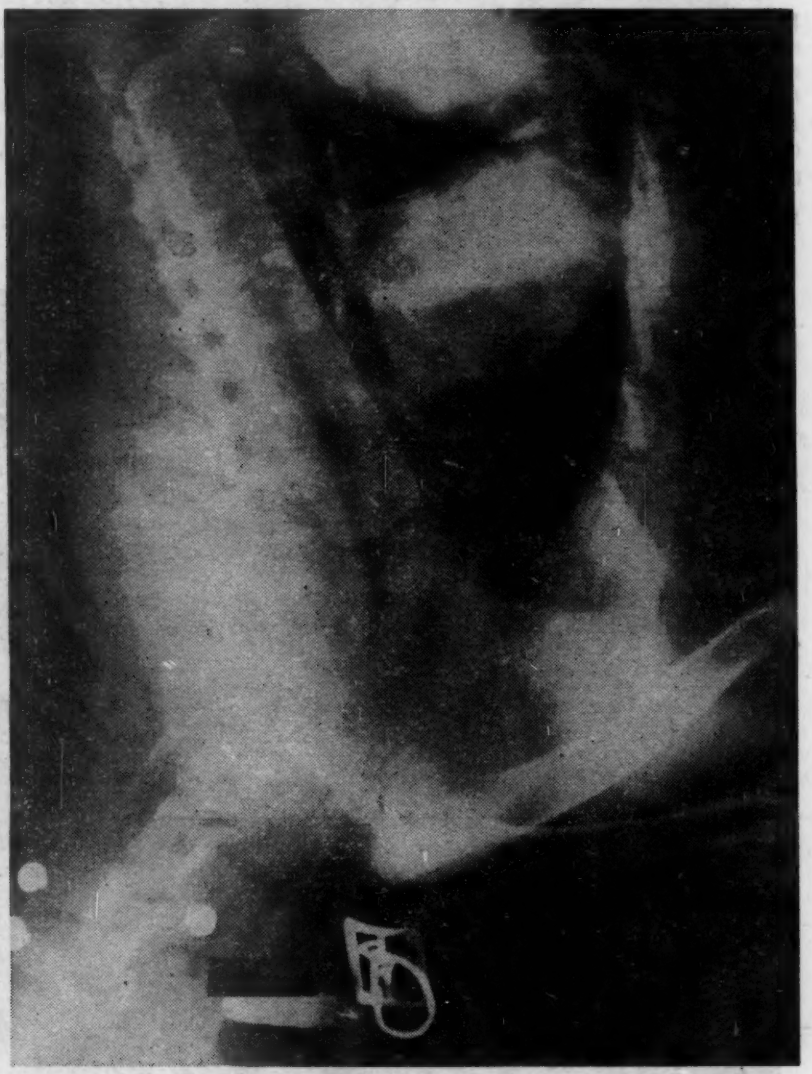
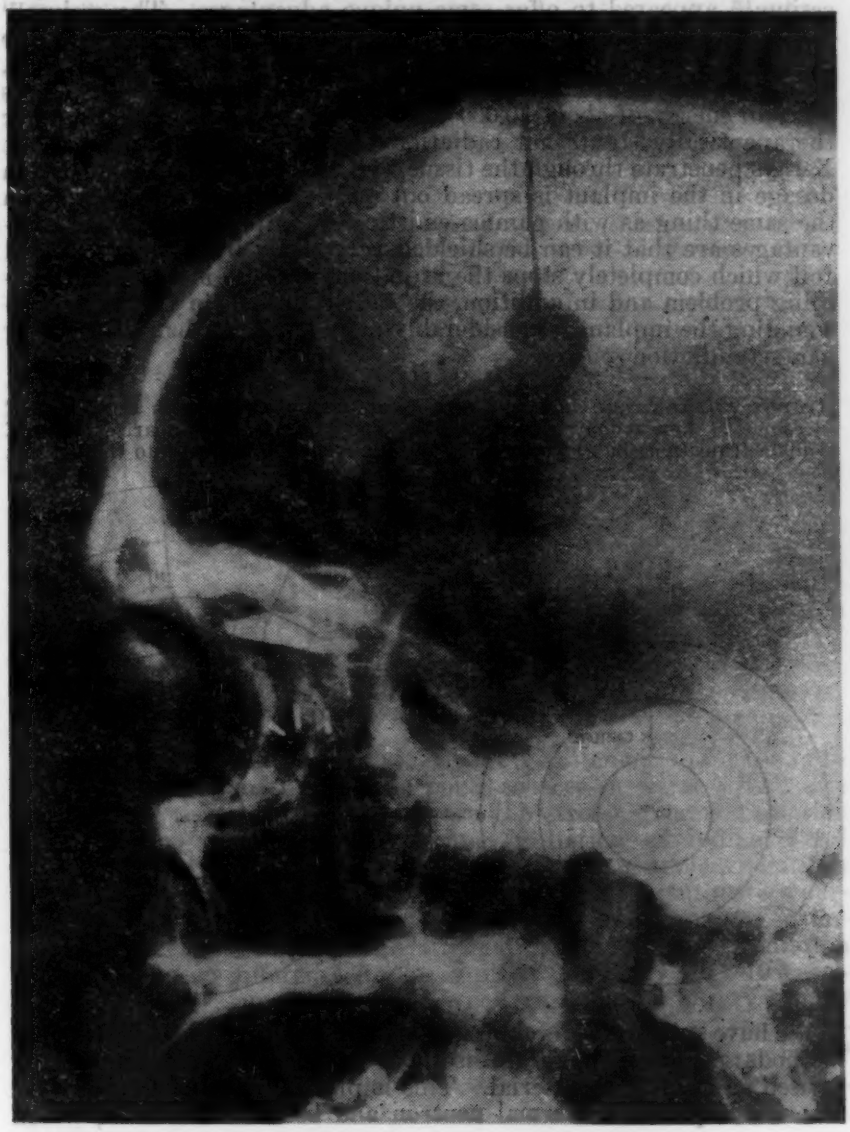


EXHIBIT 222. Plane applicator in the mediastinum of a dog.

Exhibit 223 demonstrates the clinical use of the implant in a patient with a cancer of the ethmoid sinus which invaded through the floor of the skull. The neurosurgeons removed the intracranial part of the tumor and placed an applicator over the point where the tumor was invading the skull. Radon seeds were put into the tumor below through the nose.

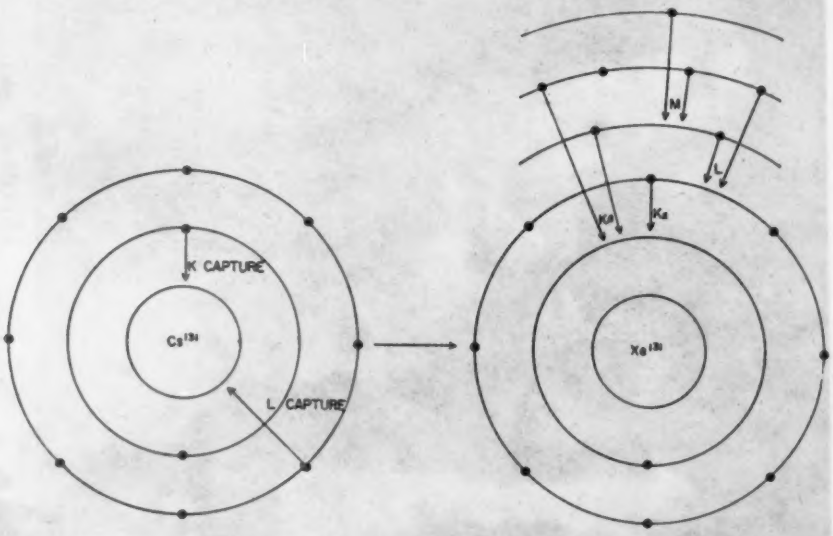
EXHIBIT 223. Plane applicator in anterior cranial fossa of a patient who had tumor of ethmoid sinus invading the cranial cavity. Radon seeds were introduced through the nose into the lower part of the tumor. The tubing through which the isotope was introduced is visible crossing the decompression defect.



Let us consider what type of isotope to use in implants of this sort. Using an isotope in solution gives a considerably greater freedom of choice, as many more isotopes are thus available. Currently we are using radioactive iodine because it has satisfactory gamma radiation, is cheap, readily available, and has suitable chemical properties for concentration to the small volume necessary for use in a tubing implant. The concentration has to be quite high in this application (of the order of 1 curie per cubic centimeter of solution) in order to reach the required linear density of about a millicurie per centimeter of tubing.

In searching through the isotope tables for other suitable isotopes, cesium[131] appeared to offer some unique advantages. The cesium[131] nucleus captures an orbital electron (exhibit 224), and leaves the resulting xenon atom with a gap in the K or inner electron shell. Electrons fall in from outer shells to fill this gap and soft X-rays with an energy of about 30,000 volts are emitted. There is no other therapeutically significant radiation from this isotope. These soft X-rays penetrate through the tissue well enough so that the radiation dosage in the implant is spread out evenly and accomplishes much the same thing as with gamma-emitting radiation sources. The advantages are that it can be shielded very easily by a very thin lead foil which completely stops the radiation, so there is almost no handling problem and in addition, the radiation field in the tissue surrounding the implant is considerably more localized than when using gamma radiation sources.

EXHIBIT 224. Diagram showing electron capture as it occurs in the decay of cesium[131]. Approximately 80 percent of the useful radiation arises from K alpha transitions in which an electron falls from the L shell into the K shell.



We have spent considerable time and effort working out production methods and dosimetry for this isotope. Naturally occurring barium[130] is used as a starting material. This is placed in the nuclear reactor where it captures a thermal neutron and becomes barium[131], which

decays with a 12-day half-life to cesium[131], the isotope with which we are concerned. This decays with a 10-day half-life by K capture, ending as xenon [131] (exhibit 225).

EXHIBIT 225. Reaction for production of Cs^{131} from Ba^{130}.

$$Ba^{130} \xrightarrow{n,\gamma} Ba^{131} \xrightarrow[12d]{K,\gamma} Cs^{131} \xrightarrow[10d]{K} Xe^{131}$$

$$1\% \quad \sigma = 5.2$$

Exhibit 226 shows the method used for separation of the daughter cesium[131] from the radiated barium. Approximately 1 mole of barium is irradiated for a month in the pile and is then melted at 700° C in an atmosphere of helium. The cesium rapidly distills off onto the aluminum cold finger from which it is easily removed with dilute nitric acid for further handling. We have processed curie quantities of Cs^{131} in this way without difficulty.

EXHIBIT 226. Device for separating carrier free daughter cesium[131] from the irradiated metallic barium by distillation at 700° to 800° C. in an atmosphere of helium.

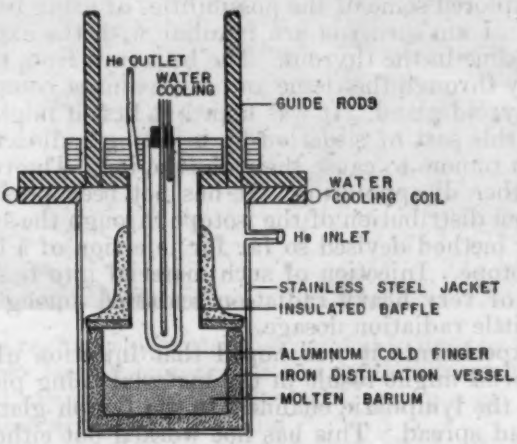
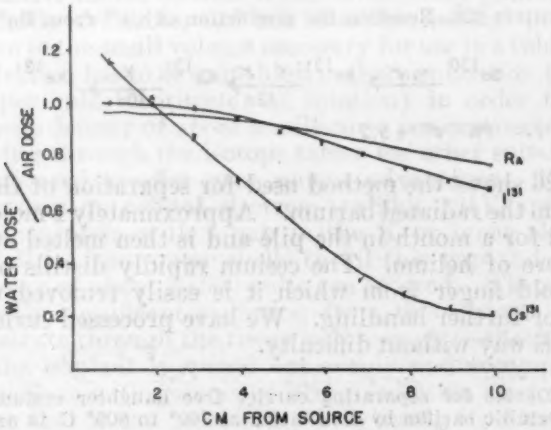


Exhibit 227 shows the measurements of the attenuation for the radiation fields surrounding various point sources in water which acts similarly to tissue. We can compare the strong gamma radiation from radium with a weaker gamma radiation of iodine[131] and soft X-rays of cessum[131]. The I^{131} and radium gamma radiations are very similar in their effects, and in the 2 to 4 centimeters surrounding the source, the region with which we are concerned in implant work, there is not enough attenuation of the cesium radiation to make a great difference in the implant dosimetry. At 10 centimeters from the source, however, the cesium radiation is very largely absorbed. This results in a much greater localization of the radiation field around the implant. Experimental implants using cesium[131] have been made and its clinical use is contemplated in the near future.

EXHIBIT 227. Diagram showing the water/air dose ratios surrounding point sources of radium, iodine[131], and cesium[131]. These demonstrate approximately the degree to which the various radiations are attenuated by scattering and absorption in tissue.



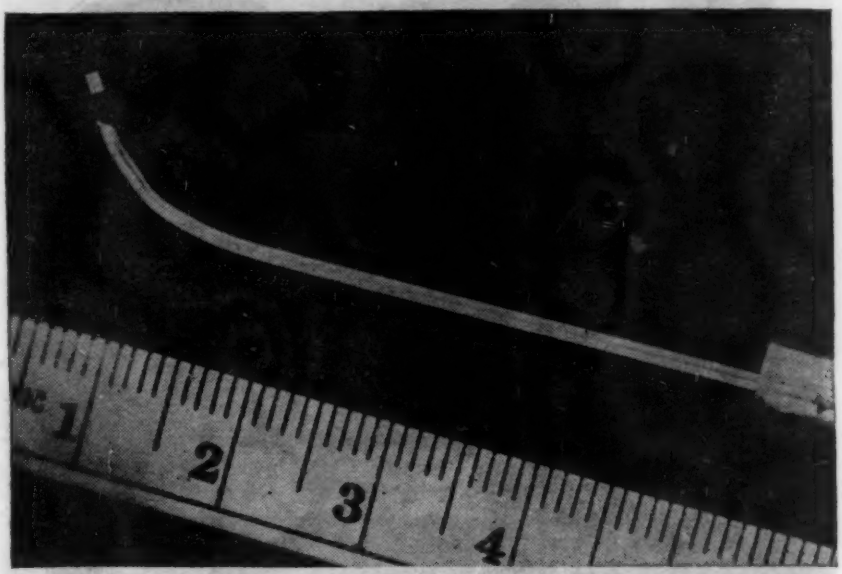
We have explored some of the possibilities of using beta rays emitting isotopes. I am sure you are familiar with the experience with radioactive iodine in the thyroid. The beta rays from the iodine are spread evently through the tissue and cause almost complete destruction of the thyroid gland. It was hoped at first it might be possible to reproduce this sort of situation by injecting radioactive colloidal materials into tumors to cause their destruction. The results of this have been rather disappointing. It has not been possible to get a sufficiently even distribution of the isotope through the substance of a tumor by any method devised so far for injection of a colloidal suspension of isotope. Injection of such material into tissue results in patchy areas of very heavy radiation scattered among areas which receive very little radiation dosage.

In other experiments it was hoped that injection of radioactive colloidal material might result in the material being picked up and carried along the lymphatic channels to the lymph glands to which tumor cells had spread. This has not worked out either. The colloids go to the lymph nodes very well, except when they contain cancer cells which block the flow of lymph. Thus the normal lymphatics receive heavy radiation but the lymphatics containing tumor escape completely.

There are, however, two applications which may prove to be useful. We have made use of the fact that when a collection of beta-emitting isotope exists in tissue the tissue surrounding it becomes completely

destroyed. Exhibit 228 shows one of the beta ray sources that we have used for destruction of tissue in this way. This is a small ceramic radioactive yttrium (Y^{90}) pellet which is handled in a shielded needle. Exhibit 229 shows the effect this has on brain tissue in the normal cat. Complete destruction of tissue was produced for a distance of about 3 millimeters and only slightly beyond this the tissue appears entirely normal. By this means we can destroy small and very well demarcated regions.

EXHIBIT 228. A ceramic radioactive yttrium oxide pellet and the shielded No. 17 needle which is used in handling it.



One of the regions it is sometimes helpful to destroy is the pituitary gland. It has been demonstrated clearly that many cases of cancer of the breast can be markedly alleviated, and in some cases forced to regress by destruction of this gland.

In the hands of our neurosurgeons it has proved to be quite difficult to remove the gland completely and they were led to seek some other method. It was thought that with implantation of sources of this sort it would be possible to destroy the gland, and it was felt that it would be possible to control the location of the radiation field much better by using descrete sources than with the injection of col-

loidal material. Exhibit 230 shows such a patient. The skull X-ray shows seven radioactive sources in the implanted pituitary gland. This patient, unfortunately, did not respond and 4 weeks later it was possible to demonstrate at autopsy the extent of destruction that was achieved in this case (exhibit 231).

EXHIBIT 229. The effect of radioactive Y^{90} pellet in the brain tissue of a normal cat. The source strength was 0.2 millicuries (approximately 80 percent self-absorption in the source). Animal was sacrificed 21 days after insertion of the source. (×10)

EXHIBIT 230.—Anteroposterior and lateral X-rays of a patient in whom 7 half

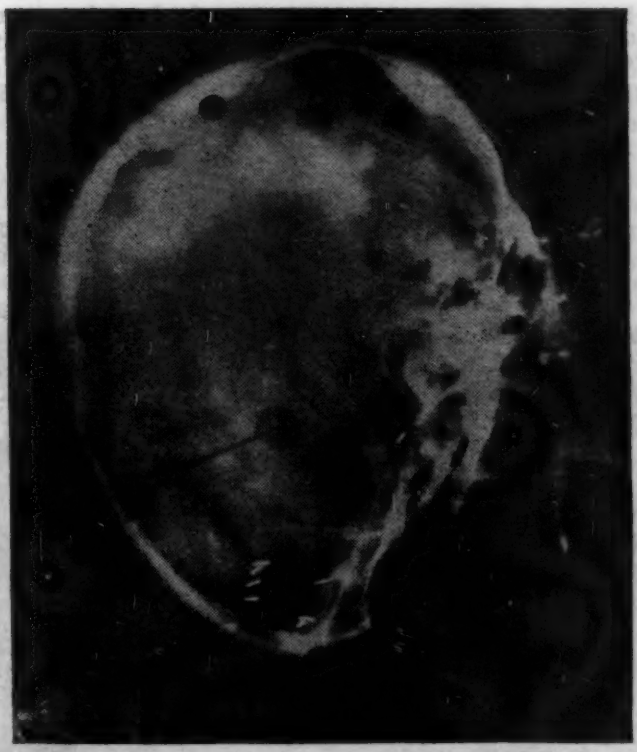


EXHIBIT 230.—Anteroposterior and lateral X-rays of a patient in whom 7 half millicurie Y^{90} pellets were inserted into the pituitary gland.

EXHIBIT 231.—Microphotograph (×10) of the pituitary gland of patient shown in exhibit 230, 4 weeks after implantation showing the degree of destruction achieved.

Representative COLE. Is the same radioactive source used irrespective of the location or growth of the tumor?

Dr. HARPER. This method is used only in cancer of the breast and the growth of the tumor is controlled by destroying the pituitary gland.

There is another application which is also properly a surgical application, I believe, in which we have found that radioactive colloidal material can be used. This is in the situation where a large cancer is taken out, for instance, of the stomach. Inevitably it is necessary to handle the tumor considerably during the course of the operation, and it is impossible to avoid in some cases spreading cancer cells

around in the abdominal cavity where they will subsequently grow. It seemed logical that when faced with this situation that if a radioactive colloidal material such as gold, or yttrium, which emits beta rays, were placed in the abdominal cavity that the invidual cancer cells spread around on the peritoneal surface should be vulnerable to this type of radiation, and it should be possible by this means to help these patients in reducing the incidence of the recurrent tumor. To prove that anything is being accomplished with this sort of treatment would require many years of study of a large series of patients, so that in this situation we turned to the experimental animal, the rat, to see if anything could be accomplished that would give us some support in carrying out the human experiment.

Exhibit 232 shows an experimental rat 2½ weeks following the injection of a suspension of tumor cells (Walker 256) into the peri-

EXHIBIT 232. Rat 17 days after the injection of a suspension of Walker 256 sarcoma cells (10^8 cells) into the peritoneal cavity.

EXHIBIT 233. Gross radioautograph of the viscera of a rat 24 hours following the intraperitoneal injection of radioactive yttrium ^{90} chloride. This material promptly becomes colloidal when it reaches body pH and acts similarly to other colloidal material injected into the peritoneum. Note the similarity of distribution between the radioactivity of the radioactive colloid and the tumor as demonstrated in exhibit 232.

A: Large amount of isotope in omentum.
B: Isotope in lymphatics of the mesentery and bowel.
C: Liver.
D: Anterior abdominal wall.
1 mg carrier yttrium in 2 ml normal saline.

toneal cavity. A great many tumor cells have apparently collected on the omentum and grown into a larger mass of tumor, and in addition there are a number of small tumor nodules scattered around on the surface of the mesentery near the bowel. The distribution of this tumor is very similar to the distribution that occurs when radioactive isotope is introduced in colloidal form into the peritoneal cavity. Exhibit 233 shows a gross radioautograph of the viscera of a rat 24 hours after the injection of radioactive yttrium ^{90}. The distribution of radioactivity is very similar to the distribution of the tumor cells. Thus, it seems that colloidal radioactive material and tumor cells that are suspended and injected into the peritoneal cavity follow similar paths, and it should be possible to kill a great many or all of the tumor cells by giving radioactive colloidal material at the same time.

This experiment in rats was carried out by giving tumor suspension followed by radioactive gold or yttrium chloride. While it was possible to prolong the lives of the animals considerably, usually an isolated tumor nodule remained somewhere as in the abdominal wall where cells had been implanted in a location inaccessable to the isotopic radiation. There seemed to be no doubt that a large majority of tumor cells are killed by a procedure of this sort, and this gives us considerable justification in attempting the procedure in human cases.

Representative PRICE. Thank you very much. That was a fine presentation, and we appreciate your cooperation with the committee.

Dr. HARPER. Thank you.

Representative PRICE. Thank you, Dr. Ely.

That concludes the hearing for this afternoon. The committee will meet again tomorrow morning in the same chamber on the fruit preservation program.

Dr. ELY. Thank you, Mr. Chairman.

(Thereupon at 3:30 p. m., Thursday, June 7, 1956, the committee recessed to reconvene at 10 a. m., Friday, June 8, 1956.)

PROGRESS REPORT ON RESEARCH IN MEDICINE, BIOLOGY, AGRICULTURE, AND FOOD PRESERVATION

FRIDAY, JUNE 8, 1956

CONGRESS OF THE UNITED STATES,
SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT,
JOINT COMMITTEE ON ATOMIC ENERGY,
Washington, D. C.

The subcommittee of the Joint Committee met, pursuant to adjournment, at 10 a. m., in the old Supreme Court Chamber of the Capitol, Hon. Melvin Price (chairman of the subcommittee) presiding.

Present: Representatives Price, Cole, and Van Zandt.

Also present: Colonel Tyron E. Huber, Chief, Medical Research Branch, Research and Development Division, Office of the Surgeon General; Dr. Ralph G. H. Siu, Technical Director of Research and Development, Office of the Quartermaster General; and Dr. Bruce H. Morgan, Deputy for Radiation Preservation, Office of the Scientific Director, Quartermaster Food and Container Institute for the Armed Forces.

Representative VAN ZANDT (presiding). The hearing will come to order.

The purpose of the hearing this morning is to receive a presentation of the Army's food preservation program.

I might say that Mr. Price, the chairman of this subcommittee, finds himself involved with the House Armed Services Committee, and he has a report to make to that group, which will explain his absence. During his absence I will act as chairman and we will proceed with the hearings.

General Hastings.

STATEMENT OF MAJ. GEN. KESTER L. HASTINGS, THE QUARTERMASTER GENERAL OF THE ARMY

General HASTINGS. Thank you, Mr. Chairman.

We recall the stout encouragement that you extended the Army delegation a year ago, when we presented our program on the radiation preservation of food. We wish to express our gratitude for your continued support and guidance as we come again before you to report on the progress of the past year and on our plans for the future.

The Army also wishes to acknowledge the participation by the Departments of State, Defense, Agriculture, Commerce, Interior, Health, Education, and Welfare, and the Atomic Energy Commis-

sion, as well as our many associates in industry and universities. Our Nation's unrivaled world leadership in this area of atoms for peace could not have been established without a closely knit team of extensive skills and enthusiastic efforts.

Last year's hearing delineated the great benefits that will accrue to both the military and civilian populations from the successful development of the radiation preservation of food. It was your desire that the Army pursue this goal with all the vigor at its command.

The Army recognized, at that time, that industry was not ready to venture capital for this necessarily high-risk research. It was also evident that eventual benefits could be realized only through the actual employment of the radiation process within the productive environment of a free economy itself. It would appear that the Army can best serve the Nation by adopting two managerial guidelines:

(*a*) Decreasing the element of technical risk, by underwriting the solution of expensive and uncertain research, and

(*b*) Phasing the program as rapidly as possible into the civilian and the free economy, by release of experimental data and encouraging joint attacks on research problems of mutual interest.

Considerable progress has been made and gratifying results have been realized. Col. William D. Jackson, Chief of Research and Development of the Army Quartermaster Corps, will now expand on the specific nature of the progress during the past year.

He will be followed by Lt. Col. Truman Cook, who will present future plans, and then monitor such questions as the committee desires.

Colonel Jackson.

STATEMENT OF COL. WILLIAM D. JACKSON, CHIEF, OFFICE OF RESEARCH AND DEVELOPMENT, OFFICE OF THE QUARTERMASTER GENERAL

Colonel JACKSON. Mr. Chairman and members of the subcommittee, I shall cover the two points General Hastings outlined to show you what we have accomplished during the past year toward—

(*a*) Reducing the technical risk for eventual commercialization of the radiation preservation of food, and

(*b*) Phasing the program into the civilian and free economy.

As far as reduction of technical risk is concerned, let us refer to our brochure (p. 318), exhibit No. 234, and also the chart which Dr. Siu can uncover for you, which lists the pertinent technical questions. I shall discuss what has been done during the past year under each case.

(A) ARE RADIATION SOURCES AVAILABLE?

(1) To date, the radiation preservation of foods project has satisfied its radiation source needs by utilizing spent-fuel assemblies, cobalt 60 sources, and electron accelerators. The project is rapidly approaching the saturation point insofar as present radiation sources are concerned. It has become increasingly evident that a facility must be constructed which will be capable of processing foods on a pilot-plant scale in order to continue essential research and development studies and to determine the economic feasibility of the process. At the present stage of knowledge, it is desirable to utilize the potentialities

of machine-accelerated electrons as well as reactor-produced gamma radiation since data indicate that each type of radiation will have its place and limitations.

(2) Gamma sources: The Atomic Energy Commission has considered the several ways in which gamma rays could be made available. Under this project gamma energies from fuel elements and cobalt 60 sources have been used for irradiation of food. Experiments utilizing the various types of sources submerged in water and in air surrounded by cooling coil and shields have yielded much valuable information.

It now appears that a gamma-producing reactor is quite feasible. The Atomic Energy Commission has budgeted for the design and construction of such a reactor—the first of its kind in the world. This will be ready by October 1958 for pilot-plant research on the radiation preservation of food.

(3) Beta sources: The technology has expanded to such a point that we now feel certain that electron generators can be produced for commercial scale processing of food. The Army has completed the specifications for an approximate 20-million-electron-volt, 60-kilowatt linear accelerator, and invitations to bid have been sent to prospective manufacturers. When completed, this generator will (to the best of our knowledge) produce more electrons in a pure stream than any other electron generator in the world. This, too, will be available for pilot-plant research in approximately 2 years.

Representative COLE. Mr. Chairman, this might be an appropriate place for me to inquire of Colonel Jackson, first, with respect to the research reactor for food preservation that you have had under consideration for the last year.

First, can you discuss it in open meeting all right?

Colonel JACKSON. Yes, sir; there is nothing classified. The Quartermaster and the Army can discuss any of this program we have. There may be some design features of the Atomic Energy Commission, but it has not been completely designed, so we do not know all the details. It is entirely unclassified at this time.

Representative COLE. I desire to go more fully into the status of the reactor for research in food preservation. Which one am I talking about? Am I talking about the gamma reactor?

Colonel JACKSON. Yes, sir.

Representative COLE. And not the beta?

Colonel JACKSON. That is correct. The reactor is a gamma producing. It is true, it does produce some beta rays, but it will optimize the production of gamma rays. The Atomic Energy Commission has in its budget for fiscal year 1957 $3 million to design and construct such a reactor for use at a suitable site when it is selected.

The beta linear accelerator I am talking about is a machine without producing the kinds of nuclear radiation you would get from various fission products. It is an electron generator.

Representative COLE. I understand a group or committee has been established for liaison between the Quartermaster and the Atomic Energy Commission to determine the criteria for selection of site for this reactor.

Colonel JACKSON. There has been.

Representative COLE. What is the progress of the work of that committee?

Colonel JACKSON. The work of that committee at the present time is under the chairmanship of the manager of the Schenectady AEC operations office. They are now surveying some 50 possible locations. They have spent about a month getting the criteria established for the location.

Representative COLE. What is the criteria?

Colonel JACKSON. The criteria is—Ralph, do you have that paper with you on the criteria?

Dr. SIU. I do not have the paper, Colonel, on the criteria. But essentially, the most important single criterion is the matter of reactor safety. The reactor safety requirement depends upon the rereactor design proper. At the present time, since the reactor design proper has not been finalized in its fullest detail, there are certain assumptions made as to the safety zone that is required around the reactor.

Now the second class of criteria involves the purpose of facility, namely, a pilot plant for research on the irradiation of food. Proximity to certain food-producing areas would be important. Proximity to transportation within a certain time from the food producing area would be important inasmuch as we would want to work with fresh produce. Those three things are the most important criteria.

Representative COLE. Three? I only got two.

Dr. SIU. Two. Excuse me, sir. Thank you for the correction.

Then the matter of whether or not technical people are available in the neighborhood for laboratory research consultation represents, you may say, a subordinate type of criteria.

Representative COLE. Then, with respect to the first point, the location has no bearing, I judge. That is, safety is the predominant factor, and that is settled by the design of the reactor itself. Therefore, geography has no bearing on point No. 1.

Dr. SIU. It does in the way of population density, of course.

Representative COLE. Then your statement that safety is fixed by the type of reactor is not completely accurate. It must be the type of reactor selected plus isolation?

Dr. SIU. That is right.

Representative COLE. Those two things.

Dr. SIU. I meant safety from the standpoint of a localized plot of land. In other words, a plot of land has to be smaller than a certain safe minimum size in which people must not live within a certain distance of the particular reactor site suggested.

Representative COLE. With respect to point No. 2, which is an area in which a variety of foodstuffs are produced upon which experimentation will not take place, what types and varieties do they have in mind? There are some sections of the country that produce nothing such—I am thinking of up in the northern section we are able to produce nothing in cotton and tobacco and so forth, and out in the Midwest they produce none of the fruits. So how are you going to pick any one locality that has all of the foodstuffs and fibers and edibles that are produced in this country?

Colonel JACKSON. One of the methods which we are using, which I can explain to you, is this:

We took a map of the United States and established certain criteria that we wanted. There are certain selected foods that look more favorable at this time. We took those foods, and we wanted to get a maximum growing season of that class of food so it would be available the longest period of time.

Representative COLE. What are the foods?

Colonel JACKSON. Well, we have various types of vegetables, such as broccoli, string beans, peas, corn, potatoes. We did not consider flour because we can ship it anywhere. It should be close to some meat-producing area, which is pretty general throughout the country, which is not a major factor in deciding.

Poultry, fish—we listed about 20, and then said the location must meet at least 12 of these.

We then plotted that on the map and took the Department of Agriculture reports of the producing areas and the length of time they are produced for these particular foods, and plotted them on the map, and we came up with patterns, which followed in the area of California, certain areas of California; the area around Maryland-Delaware up into Pennsylvania. That general area. We started to center up in there.

There are other places down near Florida, places down in Texas. Not too much in the Middle West under that criteria. Mostly toward either the eastern seaboard or the Pacific.

Representative COLE. What do Maryland and Pennsylvania produce which New York does not produce?

(Colonel Jackson laughed.)

Representative COLE. I suggest you scratch your head with both hands instead of just one.

Colonel JACKSON. I would like to be able to answer that, sir, but I cannot. I can get the data. I do not know the answer. I can establish that. There may be some difference as to lengths of growing time. In most parts of the country you can grow certain things some time of the year, but we are looking at the maximum length of time to make the plant as economic to operate as possible, because we are trying to establish economic factors. And in a food-producing area in certain seasons of the year—in summer you can grow most vegetables almost anywhere in the United States where you have good water and soil.

Representative COLE. What will be the number of personnel involved in this activity?

Colonel JACKSON. There are various estimates. About 125 people.

Representative COLE. Do you have any idea of the land area involved?

Colonel JACKSON. We would like to have——

Representative COLE. To get the necessary isolation.

Colonel JACKSON. About an area of at least 500 yards to a mile. A half a mile radius.

Representative COLE. Why was the AEC manager of the Schenectady operation selected as chairman?

Colonel JACKSON. The Atomic Energy Commission desired that they decentralize that task to a manager of one of their operations offices, who then has the assignment for that particular project. This does

not indicate that it necessarily is the place it would be located. I do, not know why that particular one was selected.

Representative COLE. Are you on the committee?

Colonel JACKSON. No, sir, I am not.

Representative COLE. Who represents the Army?

Colonel JACKSON. Colonel James, Dr. Harvey, Mr. Gramm. And there are four members from the Atomic Energy Commission.

Representative COLE. You do know, or don't you know, whether the committee has under consideration the advisability of locating this on the old airbase at Sampson.

Colonel JACKSON. The Sampson Air Force Base is on the list; yes, sir.

Representative COLE. It is?

Colonel JACKSON. Yes, sir, it is. It is in one of the lists. In fact, I think that some of the men—I have not seen the report, but they did visit Sampson Air Base. It is under consideration.

Representative COLE. When will this determination be made; do you know?

Colonel JACKSON. We expect to have it by the end of this year.

Representative COLE. I think that covers what I have in mind. Your statement indicates that the facility will be in operation by the calendar year 1958.

Colonel JACKSON. Our target date is October 1958 to be completely constructed so we can then start to operate. Quite a bit of time will be necessary in adjusting equipment and getting set up, but the construction will be finished by that date.

Representative COLE. One of the factors of the criteria of locating this facility, I judge, is not a readily accessible market for your production

Colonel JACKSON I would not say that; no, sir

Representative COLE. It is one thing to expose the various foods to radiation in varying quantities, varying degrees of exposure, and then it does not mean anything unless you try them out on people.

Colonel JACKSON. True.

Representative COLE. That is what I meant by "market for your production."

Colonel JACKSON. We figured after it is irradiated, then we plan on shipping it in our regular—I mean, running various experiments with the idea it would go into similar channels of distribution we have now.

Representative COLE. What distribution do you have other than out in Colorado?

Colonel JACKSON. As I understand your question, within the military services the quartermaster handles the distribution of foodstuffs, and we distribute normally for an economy near the buying area. We store and then distribute as needed to our men.

Representative COLE. Then, Colonel, I misunderstood completely the purpose of this facility. I thought it was for research.

Colonel JACKSON. It is.

Representative COLE. Then what are you talking about putting your radiated foods into the quartermaster channels of foodstuffs? You are not going to do that certainly.

Colonel JACKSON. No, sir; not at this time. Perhaps we are both on two different premises. As I understood your question, you said, "How are you going to get food into distribution?"

Representative COLE. I meant the market of your food and research is the human body, the people who have exposed themselves to consuming it.

Colonel JACKSON. Yes, sir.

Representative COLE. So I judge that is not an element of concern to you, because it is not necessary for the people who are to sample it to be right close by or in the proximity of the research reactor.

Colonel JACKSON. That is correct.

Representative COLE. They can either be brought into the nearby municipality or the foodstuffs shipped to wherever they may be.

Colonel JACKSON. That is true.

Representative COLE. Is it intended that the foods that are exposed in this facility will be tested, sampled, only out at Colorado Springs by human beings?

Colonel JACKSON. No, sir. This is the beginning of a plan to bring into commercial usage, and right today we are irradiating—let us take an example of what we are doing today. We are irradiating food at Arco, Idaho, and shipping to Denver, which you are familiar with, where it is sampled by a very small group.

We visualize that after certain criteria have been established we must test it on large groups of people. The food will be shipped from the plant to the people, not the people to the plant.

Representative COLE. Have you reached the point in your research with respect to any food item in which you are now prepared to deal it out to human beings in large quantities?

Colonel JACKSON. No, sir; we have not reached that point.

Representative COLE. When do you think you might?

Colonel JACKSON. The schedule is, as I remember it, 1960. By 1959 we expect to have some foods, but user testing and clearances we expect to have completed by 1960 and to start troop-consumption experiments at that time.

Representative COLE. In your program is there any other place than Denver at which you plan to conduct experiments in consumption of the foods?

Colonel JACKSON. Yes, sir.

Representative COLE. Where is that?

Colonel JACKSON. They have not been established at this time.

Representative COLE. Do you know how many there will be?

Colonel JACKSON. Perhaps——

Representative COLE. If it is experimental, why is it necessary to have more than Colorado? Why is not Colorado enough to take care of all of your testing requirements?

Colonel JACKSON. We plan on, for example, troop-acceptability tests. We had planned initially perhaps we would test food at Fort Lee, which is one of our own installations, and after that it would be tested at other military installations after we had established the basic clearance of the Surgeon General, and that has not been established. So we have not planned too far ahead into that.

Representative COLE. Then we are using the word "test" in different meanings. I am talking about the type of work you are doing at

Denver. Do you intend duplicating, doing the same kind of work in other medical institutions, hospitals, in the country?

Colonel JACKSON. Perhaps I had better ask Colonel Huber, who is the Surgeon General's representative and knows that field far better than I. I do not think he does.

Colonel HUBER. No, sir; we do not plan to duplicate those facilities, sir. In the first place, they are rather expensive, to set up a metabolic ward, which is what you are talking about.

Representative COLE. Yes.

Colonel HUBER. We have these 10 subjects out there, and thus far we have kept up with the Quartermaster General's getting us foods that we can test. It might be possible to enlarge that if we get behind, but we have not gotten behind so far.

Representative COLE. That could be, because the quartermaster production facility is limited.

Colonel HUBER. It may be.

Representative COLE. When he gets through planning and into operation he may be pushing food at you faster than you can handle it.

Colonel HUBER. We can double the facilities.

Representative COLE. You can double it?

Colonel HUBER. Yes, sir.

Representative COLE. At Denver?

Colonel HUBER. Yes, sir.

Representative COLE. Are you having any difficulty in obtaining sufficient number of subjects?

Colonel HUBER. No, sir; not a bit.

Representative COLE. Is there an oversubscription?

Colonel HUBER. I do not know just how to answer that question, sir. We have had subjects go back to their hometowns and, shall I say, subscribe others to come to our program. We have 25 or 30 report to us, and we have to examine those and turn back about half of that because they do not meet our special qualifications as to age or health or something like that. But we have had no difficulty getting subjects.

Representative COLE. And you do not anticipate any shortage of personnel, subjects, even though the amount of food to be tested may be increased substantially?

Colonel HUBER. If they do bring us more foods than they have in the past, we could expand our facility a hundred percent tomorrow.

Representative COLE. Thank you, Colonel Huber.

Colonel HUBER. Yes, sir.

Representative COLE. Now, Colonel Jackson, this particular reactor is initially for research purposes.

Colonel JACKSON. Yes, sir.

Representative COLE. Is it the thinking of the Quartermaster people that it will also be used for commercial purposes, that is, to irradiate foods which are to be distributed in the channels of the Army?

Colonel JACKSON. What we visualize, Mr. Congressman, is this: At the present time we are quite limited in what we can irradiate, so we want a facility that will give us sufficient food so that we can meet all the requirements for our wholesomeness studies and all the research in that field, and to run what we call user tests, which are tests by military people in eating just like it is regular food, and see how that works. These would be fairly large-scale tests where you would

use maybe as many as a thousand people at a time in an experiment. This facility, we visualize, will be contractor operated. It will be controlled by the Army, but we plan on doing it by contract. It may well be, because this is the initial plan of this type, that we would have to service some other industries and do things for commercial people for them to merchandise any way they see fit until they can build equipment of their own. And we do that today on a very, very small scale, which I will cover a little later, the number of people that we have that we are presently irradiating for for them to do research experiments. But that could grow very well if their research is as successful as it indicates. It could run into considerable volume.

We are not building a plant with that in mind, because when we have finished our work it is not our position that we will stay in the food-processing business, if that is one of the questions which you desired answered.

Representative COLE. Thank you.

Representative VAN ZANDT. At the present time you are using facilities at the Argonne Laboratories to radiate your food. Is that correct?

Colonel JACKSON. Yes, sir; we are. We are using Argonne National Laboratories, we are using the materials testing reactor in Utah, we are using General Electric's facilities, we are using the applied radiation facility in the west coast, and we are using the high-voltage engineering, and then we are using facilities at Massachusetts Institute of Technology, Michigan, Stanford Research Institute, University of Chicago. Many of the universities that have contracts also have facilities put there by agreements with the Atomic Energy Commission, and we are utilizing those wherever possible because it makes a simpler way of administering the research.

Representative VAN ZANDT. In connection with this proposed reactor, no doubt you are familiar with the fact it has already been authorized?

Colonel JACKSON. Yes, sir. We have been informed, and we also have been informed they are working on the design at this time.

Representative VAN ZANDT. Is it not true that the manager at Schenectady at the AEC probably was given this responsibility because of the possibility that General Electric will design the reactor?

Colonel JACKSON. I am not familiar with that. I do not know. I cannot answer that.

Representative VAN ZANDT. Thank you. You may continue with your statement.

Colonel JACKSON. Are irradiated foods wholesome?

The Department of the Army has conducted intensive tests on the nutritional adequacy of irradiated foods. We have observed that the energy value of several meat, vegetable, and dairy products tested thus far has remained unaltered by irradiation. The destruction of vitamins is, in general, not greater in processing foods by radiation sterilization than by heat treatment.

Data thus far obtained from animal-feeding experiments do not indicate any production of toxic compounds by radiation sterilization or preservation.

Representative VAN ZANDT. Referring to your statement:

The destruction of vitamins is, in general, not greater in processing foods by radiation sterilization than by heat treatment.

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. What do you lose when you cook foods in the way of vitamins?

Colonel JACKSON. I will have to turn to my nutritionist, Dr. Siu, to answer that. I think you lose around 40 percent as a guideline.

Dr. SIU. In certain cases you lose an excessive amount. The percentage may vary from 10 percent up to, say, 80 percent.

Representative VAN ZANDT. What percentage is lost when food is irradiated?

Colonel JACKSON. In this little handout which is in part of this folder we have a table which shows specifically that with thiamine, by heat treatment, there is a destruction of 65 percent, and by radiation sterilization a destruction of 63 percent. So it is very close.

Representative VAN ZANDT. It runs about even, does it not?

Colonel JACKSON. It varies, though, with each vitamin. Riboflavin, by heat treatment, there is a loss of 20 percent, and by radiation sterilization a loss of only 8 percent. That is on page 5 of this little booklet of the Surgeon General.

Representative VAN ZANDT. Would you make available to the reporter this table so it can be inserted in the record at this point?

Colonel JACKSON. Yes, sir.

(The table referred to follows:)

Comparative data on vitamin destruction in foods

Vitamin	Heat treatment	Radiation sterilization
	Percent	*Percent*
1. Thiamine	65	63
2. Riboflavin	20	8
3. Pyridoxine	30	25
4. Niacin	30	0-3
5. Folic acid	35	0
6. Vitamin E		[1] 10-30
7. Vitamin A	20	[1] 8-20

[1] 80,000 r/hour on dairy products.

Representative COLE. I would like to ask, under your No. 2 item, Colonel, you say that the animal feeding experiments do not indicate any production of toxic compounds by radiation sterilization or preservation.

Colonel JACKSON. Yes, sir.

Representative COLE. What do you mean by that?

Colonel JACKSON. There are many uses for this type of energy, and when we talk of sterilization or commercial sterilization it means that a product is similar to a canned product, that you have it sterilized to the point where you can store it, and it will last a reasonable length of time in the matter of years perhaps, and no bacterial growth will occur.

Representative COLE. When you use the expression "preservation" you are referring to other methods of preserving food than radiation sterilization?

Colonel JACKSON. More of a temporary nature.

Representative COLE. I am only trying to find out what you are talking about.

Colonel JACKSON. Yes, sir.

Representative COLE. What do you mean when you say "preservation"?

Colonel JACKSON. Low dose rates, sir, is what we are talking about in this project, and at the low dose rates you do not kill all of the bacteria, but you can kill most of them. And the reason——

Representative COLE. When you say "preservation" you are refering to the process of irradiation?

Colonel JACKSON. Yes, sir.

Representative COLE. Oh.

Colonel JACKSON. Yes, sir. This refers only to preservation or sterilization by irradiation.

Representative COLE. In both cases?

Colonel JACKSON. Yes, sir.

Representative COLE. I see.

Colonel JACKSON. I am sorry.

Representative VAN ZANDT. Colonel, is it not true that you package and also can food?

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. By irradiation you simply extend the life of the contents of the food in the can?

Colonel JACKSON. The food must be packaged so it cannot be recontaminated from the air.

To continue: Repeated measurements and theoretical calculations reaffirmed that irradiated foods are not radioactive at any of the energies used.

Four series of human volunteer feeding studies have been completed. They were started on May 9, 1955, the day on which we presented our program to you last year. Human volunteers were fed diets of which the irradiated components provided 35, 65, 85, and 100 percent of the total calories from irradiated foods. No adverse effects of any kind were observed.

Representative VAN ZANDT. Colonel, regarding your first class of consumers of sterilized food.

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. Have they completed their tour of duty at Fitzsimons?

Colonel JACKSON. The first group, I would say, has. Perhaps Colonel Huber can answer that. The first group, it has, sir.

Representative VAN ZANDT. Have they returned to their homes?

Colonel HUBER. Yes, sir.

Representative VAN ZANDT. How frequently will they return to Fitzsimons General Hospital for observation?

Colonel JACKSON. Once every 6 months, and then once a year after the first year.

Colonel HUBER. I would like to make a correction. It is in our brochure. They return, as we suggested to in the other meeting 3, 6, and 12 months after they have completed their study. It is exhibit 6 of our brochure.

Representative VAN ZANDT. So you have a new class now?

Colonel HUBER. Yes, sir.

Representative VAN ZANDT. Ten in number?

Colonel HUBER. Ten in number.

Representative VAN ZANDT. And you have another class coming up for next year?

Colonel HUBER. Yes, sir.

Representative VAN ZANDT. Go ahead, Colonel Jackson.

Colonel JACKSON. In collaboration with the Food and Drug Administration, Department of Health, Education, and Welfare, an experimental procedure for long-term animal testing of irradiated foods has been developed. Studies on pork and potatoes irradiated and then stored at room temperature for 3 to 6 months have been initiated. Similar studies on beef and flour are scheduled in the near future.

All of the wholesomeness studies thus far affirm the safety of irradiated foods. The handout furnished you in the back of your brochure provides additional information on the subject of wholesomeness.

In addition, we have collaborated with—in this brochure there is additional information on wholesomeness. This brochure contains pictures and charts showing the wholesomeness studies that have been completed to date. We would like to offer this as one of the exhibits.

Representative VAN ZANDT. Unless I hear an objection, at this point we will make this brochure a part of the record of the hearings.

Colonel JACKSON. That is the purpose of it, sir.

(The brochure referred to follows:)

ARMY PRESENTATION ON RADIATION PRESERVATION OF FOOD BEFORE THE SUBCOMMITTEE ON RESEARCH AND DEVELOPMENT, JOINT COMMITTEE ON ATOMIC ENERGY, JUNE 8, 1956

INTRODUCTORY REMARKS BY MAJOR GENERAL HASTINGS

Mr. Chairman and members of the subcommittee, we recall the stout encouragement that you extended the Army delegation a year ago, when we presented our program on the radiation preservation of food. We wish to express our gratitude for your continued support and guidance as we come again before you to report on the progress of the past year and on our plans for the future.

The Army also wishes to acknowledge the participation by the Departments of State, Defense, Agriculture, Commerce, Health, Education, and Welfare, and the Atomic Energy Commission, as well as our many associates in industry and universities. Our Nation's unrivaled world leadership in this area of atoms-for-peace could not have been established without a closely knit team of extensive skills and enthusiastic efforts.

Last year's hearing delineated the great benefits that will accrue to both the military and civilian populations from the successful development of the radiation preservation of food. It was your desire that the Army pursue this goal with all the vigor at its command.

The Army recognized, at that time, that industry was not ready to venture capital for this necessarily high-risk research. It was also evident that eventual benefits could be realized only through the actual employment of the radiation process within the productive environment of a free economy itself. It would appear that the Army can best serve the Nation by adopting two managerial guidelines:

(*a*) Decreasing the element of technical risk, by underwriting the solution of expensive and uncertain research; and

(*b*) Phasing the program as rapidly as possible into the civilian and the free economy, by release of experimental data and encouraging joint attacks on research problems of mutual interest.

Considerable progress has been made and gratifying results have been realized. Col. William D. Jackson, Chief of Research and Development of the Army Quartermaster Corps, will now expand on the specific nature of the progress during the past year.

PROGRESS REPORT BY COLONEL JACKSON

Mr. Chairman and members of the subcommittee, I shall cover the two points General Hastings outlined to show you what we have accomplished during the past year toward—

(*a*) Reducing the technical risk for eventual commercialization of the radiation preservation of food; and

(*b*) Phasing the program into the civilian and free economy.

As far as reduction of technical risk is concerned, let us refer to brochure exhibit No. 234, which lists the pertinent technical questions. I shall discuss what has been done during the past year under each case.

(*a*) *Are radiation sources available?*

(1) To date, the radiation preservation of foods project has satisfied its radiation source needs by utilizing spent fuel assemblies, cobalt 60 sources, and electron accelerators. The project is rapidly approaching the saturation point insofar as present radiation sources are concerned. It has become increasingly evident that a facility must be constructed which will be capable of processing foods on a pilot plant scale in order to continue essential research and development studies and to determine the economic feasibility of the process. At the present stage of knowledge, it is desirable to utilize the potentialities of machine-accelerated electrons as well as reactor-produced gamma radiation since data indicate that each type of radiation will have its place and limitations.

(2) *Gamma sources.*—The Atomic Energy Commission has considered the several ways in which gamma rays could be made available. Under this project gamma energies from fuel elements and cobalt 60 sources have been used for irradiation of food. Experiments utilizing the various types of sources submerged in water and in air surrounded by cooling coil and shields have yielded much valuable information.

It now appears that a gamma producing reactor is quite feasible. The Atomic Energy Commission has budgeted for the design and construction of such a reactor—the first of its kind in the world. This will be ready by October 1958 for pilot plant research on the radiation preservation of food.

(3) *Beta sources.*—The technology has expanded to such a point that we now feel certain that electron generators can be produced for commercial-scale processing of food. The Army has completed the specifications for an approximate 20-million-electron-volt 60-kilowatt linear accelerator, and invitations to bid have been sent to prospective manufacturers. When completed, this generator will (to the best of our knowledge) produce more electrons in a pure stream than any other electron generator in the world. This, too, will be available for pilot-plant research in approximately 2 years.

(*b*) *Are irradiated foods wholesome?*

(1) The Department of the Army has conducted intensive tests on the nutritional adequacy of irradiated foods, and has observed that the energy value of several meat, vegetable, and dairy products tested thus far has remained unaltered by irradiation. The destruction of vitamns is, in general, not greater in processing foods by radiation sterilization than by heat treatment.

(2) Data thus far obtained from animal-feeding experiments do not indicate any production of toxic compounds by radiation sterilization or preservation.

(3) Repeated measurements and theoretical calculations reaffirmed that irradiated foods are not radioactive at the energies used.

(4) Four series of human volunteer feeding studes have been completed. They were started on May 9, 1955, the day on which we presented our program to you last year. Human volunteers were fed diets of which the irradiated components provided 35, 65, 85, and 100 percent of the total calories. No adverse effects of any kind were observed.

(5) In collaboration with the Food and Drug Administration, Department of Health, Education, and Welfare, an experimental procedure for long-term animal testing of irradiated foods has been developed. Studies on pork and potatoes irradiated and then stored at room temperature for 3 to 6 months have been initiated. Similar studies on beef and flour are scheduled in the near future.

(6) All of the wholesomeness studies thus far affirm the safety of irradiated foods. The handout furnished you in the back of your brochure provides additional information on the subject of wholesomeness.

(*c*) *Are irradiated foods tasty?*

As you recall from last year's discussion, the reaction of foods to radiation varies from food to food. During the past year we have surveyed over 80 foods. Quite a few of the irradiated foods show considerable promise. Typical of these are pork loin and pork sausage. The former has been demonstrated to show no noticeable change in appearance and taste after 9 months' storage at room temperature. In brochure exhibit No. 235 roast pork and roast beef stored for 5 weeks are shown, as are other products we have worked on.

Irradiated sliced bacon (exhibit 236) with a salt content comparable to the civilian product, rather than the high salt content now used in Army bacon, shows good taste acceptance after 6 months at room temperature. This same product in frozen storage has remained satisfactory three times as long as the frozen nonirradiated bacon.

Poultry (exhibit 237) results are also encouraging; table preparation of either fresh or precooked irradiated chicken, stored for 4 months at room temperature, resulted in a highly accepted product. The photograph shows samples of chicken which were either irradiated raw or precooked and stored 5 weeks at 70° F. You will notice that in the precooked sample an acceptable appearing bird is produced. This appears to be of a higher quality than the commercial whole canned chickens of today.

Studies on fish products have been expanded. Shrimp and oysters in particular, show good promise. The brochure picture (exhibit 238) demonstrates samples of oysters after 5 weeks storage at 70° F. In both methods of preparation, the product was found to be tasty. This is a product without counterpart on today's markets.

Pasteurizing doses of radiation using strawberries and grapes prolonged their storage by a factor of three in experiments designed to duplicate distribution cycle temperatures.

In the vegetable line, green beans have shown good promise.

Irradiated flour remained insect free after 9 months of storage at temperatures up to 100° F. and when used in baking bread produced loaves with normal characteristics. The results of this work varying radiation dose, storage temperature, and moisture content of the flour during storage, are shown in the brochure (exhibit 240).

(*d*) *Is the irradiation process economical?*

At the hearing last year, preliminary estimates of various workers in the field were mentioned. The current estimates are shown in brochure exhibit No. 244.

These estimates are based upon the knowledge currently available. What is needed is pilot-plant experience to arrive at a more reliable economic analysis. We have made rapid progress during the past year toward this objective. Preliminary plans have been made for the establishment of the Army Ionizing Radiation Center. This center will consist of three main parts: A gamma ray producing reactor to be designed and built by the Atomic Energy Commission, a linear accelerator to be designed and built under contract, and a food-processing pilot plant. The work is progressing according to the schedule we discussed with you last year. We have every indication that the pilot plant will be operating in the latter part of 1958. An economic feasibility study is in progress and will develop additional information which will be useful in determining prospective cost figures.

Summarizing this section of the presentation, we can say that the technical risk has been reduced considerably during the past year. The promise looks brighter than ever. I am not suggesting by such optimism that all the technical problems, or even the principal ones, have been solved. On the contrary, there is a long way to go. As a matter of fact, as research mounts into the pilot-plant stage, a new dimension of problems with increasing costs unfold.

Let us now proceed to discuss the phasing of the program into the civilian and the free economy. During the past year, we have taken determined steps with encouraging results. We have effected a wide distribution of information. We have broadened the base of knowledge. We have markedly increased the degree of active industrial participation. And we have established a formal means of Federal interdepartmental collaboration. Let us take up each of these points in turn.

(e) *Release of information (brochure exhibit No. 245)*

(1) During the past year the progress of the program has received nationwide dissemination in press, radio, television, exhibits, and speeches. Over 25 such releases have been made.

(2) Semitechnical progress reports presenting the highlights of our technical accomplishments have been distributed to an established industrial mailing list which now consists of over 350 firms. Some 4,000 pieces of literature have been distributed.

(3) The Department of the Army has sponsored open technical sessions before annual meetings of food and allied industries. Since last year we have sponsored or will sponsor programs before the American Chemical Society, Association of Food and Drug Officials of the United States, Institute of Food Technology, Research and Development Associates, Federation of American Society of Experimental Biology. Reports of contractual investigations will be published by the Department of Commerce for release to the public. Brochure exhibit No. 246 is a list of publications currently available to the public from the Department of Commerce.

(4) The Army is frequently requested to prepare and deliver oral presentations to governmental agencies as well as non-Government groups. We have participated in over 50 technical and industrial programs during the past year.

(f) *Broadening base of knowledge*

We are continuing to expand the base of knowledge. The majority of our research effort is carried out by means of contracts with universities, industry, and other research groups. Additionally a National Research Council committee, as well as a quartermaster industrial advisory committee and the Surgeon General's Advisory Committee on Nutrition, assist us in expanding the base of knowledge in the field. Brochure exhibit No. 247 lists the institutions supported last year by the Army for research in the radiation preservation of food.

(g) *Industrial participation*

To stimulate industrial interest we devised a system of no-cost-to-the-Government contract with competent industrial organizations on problems of mutual interest. In 1955, four companies participated. Last year, the number was increased to 22. These organizations are listed in brochure exhibit No. 248.

(h) *Intragovernmental collaboration*

Following a series of briefings to various Government departments last year by an Army team, an Interdepartmental Committee on Radiation Preservation of Food has been formally organized consisting of representation from Departments of State, Defense, Agriculture, Commerce, Health, Education, and Welfare, and the Atomic Energy Commission. Membership of this Committee is shown in brochure exhibit No. 249. The Committee's functions are:

(1) Provide motivation and broad guidance for the Government research program on the radiation preservation of food.

(2) Effect a transition of program responsibility from the Department of Defense to other Government agencies and to the free economy as rapidly as possible.

(3) Render a semiannual report to the President on the progress made with relation to our Nation's atoms-for-peace effort.

The first meeting was held on May 15, 1956. However, before that meeting, the following governmental agencies were actively contributing to the program.

(a) Atomic Energy Commission: Source of gamma radiation.

(b) Department of Health, Education, and Welfare: Food testing experimental procedures.

(c) Department of Agriculture: Supplementary studies (microbiological studies on food products).

(d) Department of State: United States Information Agency.

(e) Department of Commerce: Industrial education, and public information.

We can readily see that increasingly intense interest is being generated in the civilian agencies and the free economy. We are looking forward to the day when this interest reaches the point where the actual commercialization is realized. Given continued strong support from this Committee and other legislative and executive leaders, we have every hope that this will arrive within the foreseeable future.

5. With this quick survey of our progress of the past year, I would like to turn the floor over now to Lt. Col. Truman F. Cook from the Department of Army General Staff. He will describe the Army's plans for the future.

FUTURE PLANS, BY LIEUTENANT COLONEL COOK

Mr. Chairman and members of the subcommittee, from an overall analysis of the current state of the art, we believe that the days of excessive technical risk in the program of radiation preservation of food are numbered. There are still large and difficult problems ahead. But we now possess sufficient data to make a reasonable estimate of the success potential. Within a few years the specific areas of practical applications and the profit incentive to proceed should be amply evident to industry.

Accordingly, the Army is proceeding along the following lines:

(*a*) In its present role of spearheading the national effort, the Army will attempt to gradually phase out of the position of dominance. It will rely on the Interdepartmental Committee on Radiation Preservation of Food to stimulate great participation by the civilian agencies of the Government and aid in bringing about an effective transition into the free economy. At the same time we will continue to speed up the arrival of this last step by increasing the scope of no-cost collaborative arrangements with industrial concerns, by wide dissemination of research data and by spreading the base of know-how by means of research contracts.

(*b*) The Army will complete those critical phases which it began several years ago. These include studies necessary for the Food and Drug Administration clearance for a reasonable number of irradiated foods, the development of pilot-plant operational data using a beta source and a gamma source, and the furnishing of consultation and irradiation services to industrial concerns for experimental purposes for several years. The Army hopes that other agencies and industry will eventually take over such problems as the development of more accurate and convenient techniques for the measurement of high dosages of ionizing radiation, the radiation deinfestation of fruits, and the further expansion of food markets, for example, fish products.

(*c*) As the civilian and industrial interests begin to assume their own proper roles in the field, the Army will gradually concentrate on its specific logistical questions. To be sure, the two are not completely separate. Nevertheless, the degree of emphasis on various facets of the total problem will differ. In this respect, we have set up targets as shown in brochure exhibit No. 250.

1956: Survey on 80 Foods
Wholesomeness Tests—Human Feeding Tests
Inform American Businessmen
Preliminary Plans for Army Ionizing Radiation Center
1957: Begin Construction of Army Ionizing Radiation Center
Research Emphasis on 20 Selected Foods
Foreign Trade Fairs
1958: Packaging Studies
Storage and Handling Studies
Limited Troop Taste Testing
Army Ionizing Radiation Center in Operation
1959: Pilot Plant Research on 20 Foods
Pilot Plant Production on 10 Foods
Industry Assumes Larger Role
1960: User Acceptance Clearance on Some Foods
Troop Consumption Experiments
Economic Analysis for 10 Foods, Based on Pilot Plant Production Experience
Production By Industry Begins
Procurement of Few Selected Items Begins

There can be no greater expression of our optimism, Mr. Chairman and members of the subcommittee, than such a statement of definite practical target objectives. We hope you are pleased with the progress we have made over the past year under your guidance and encouragement.

Thank you very much for the opportunity to present this progress report.

EXHIBIT 234

REDUCING THE TECHNICAL RISK FOR EVENTUAL COMMERCIALIZATION OF THE RADIATION PRESERVATION OF FOOD

point 1 ARE RADIATION SOURCES AVAILABLE ?

point 2 ARE IRRADIATED FOODS WHOLESOME ?

point 3 ARE IRRADIATED FOODS TASTY ?

point 4 IS THE RADIATION PROCESS ECONOMICAL ?

EXHIBIT 235. Roast pork and roast beef cooked after storage (gamma).

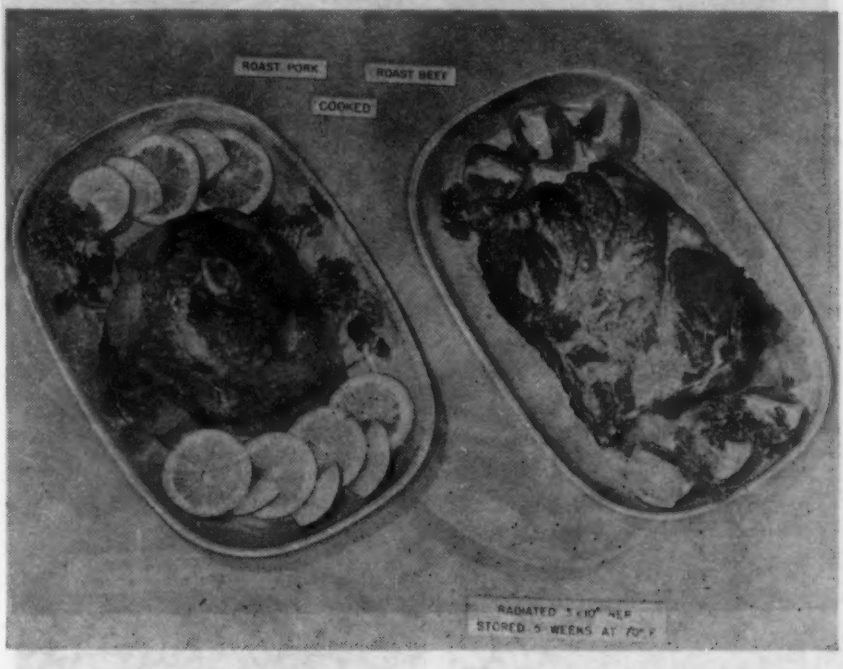


EXHIBIT 236. Sliced bacon, 4 months, frozen, gamma irradiation (no color change).

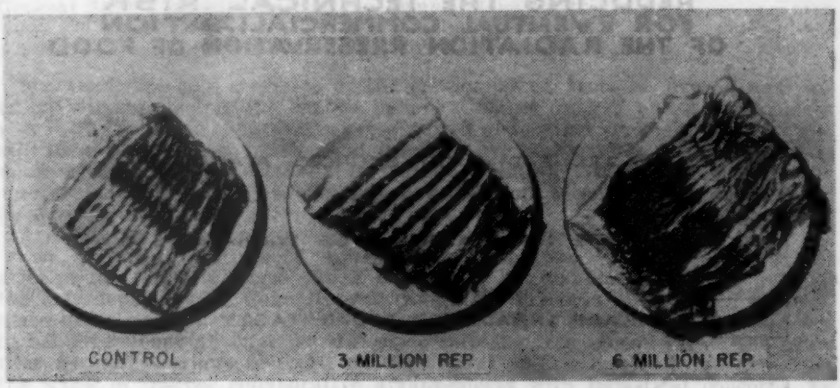


EXHIBIT 237. Chicken, fryer. Left, after irradiation (gamma) and storage. Right, sample cooked following storage.

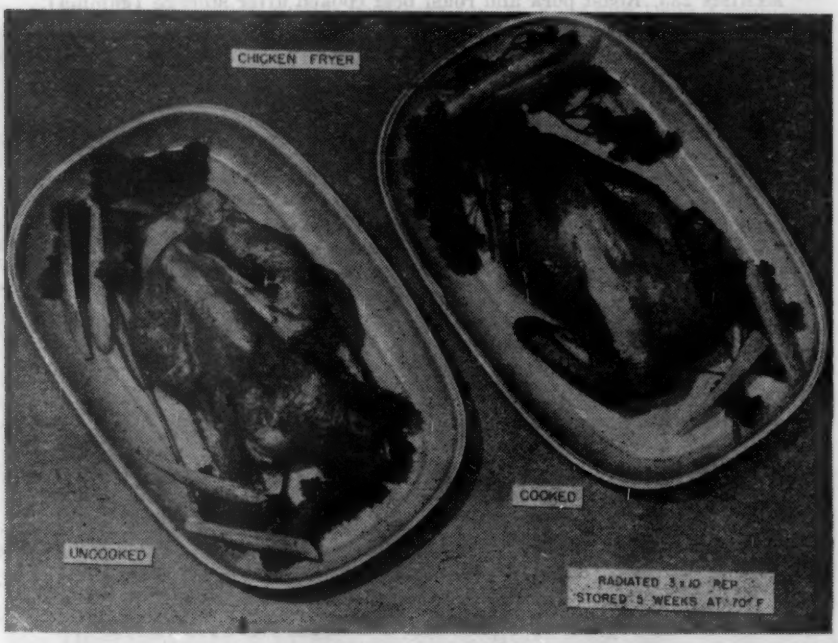


EXHIBIT 238. Oysters, fresh and fried, fried after storage.

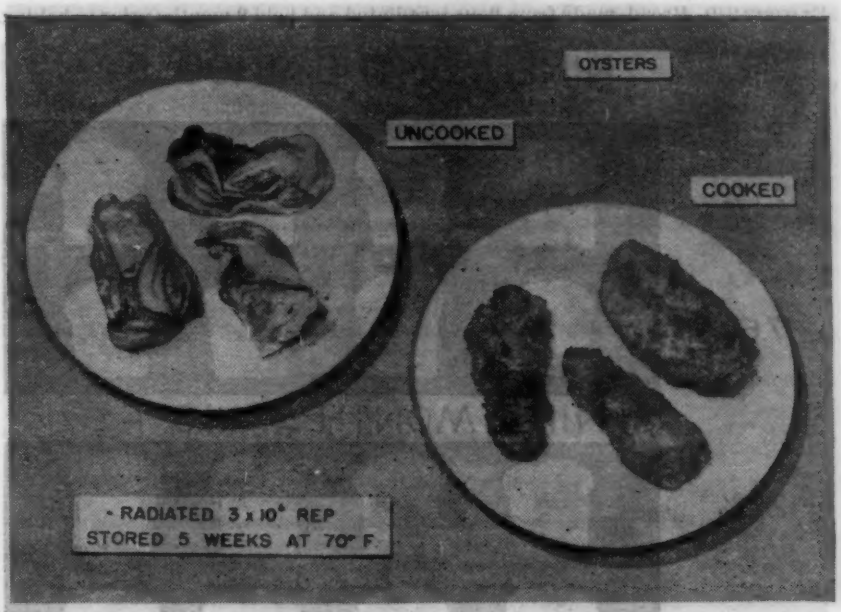


EXHIBIT 239. Artificially infested wheat (granary weevils). Left, 100,000 rep (electron), 43 days room temperature. Right, not treated.

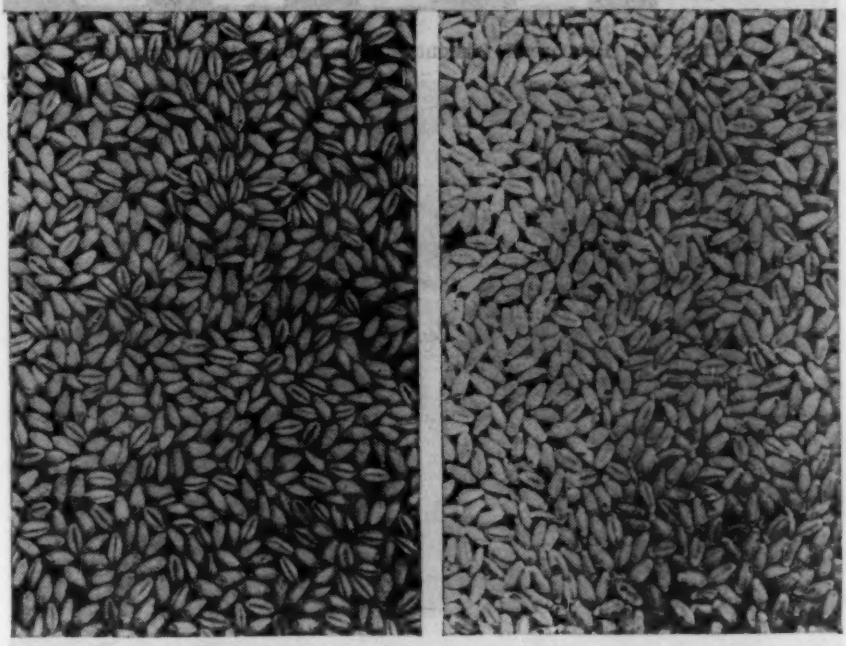


EXHIBIT 240. Bread, made from flour irradiated and held 9 months prior to baking.

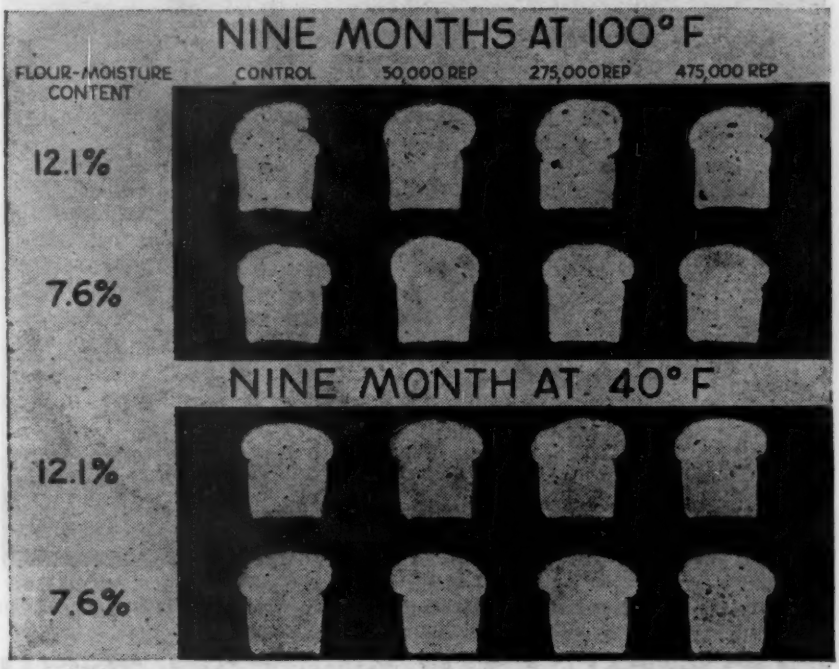


EXHIBIT 241. Rye bread, 2 months room temperature (gamma).

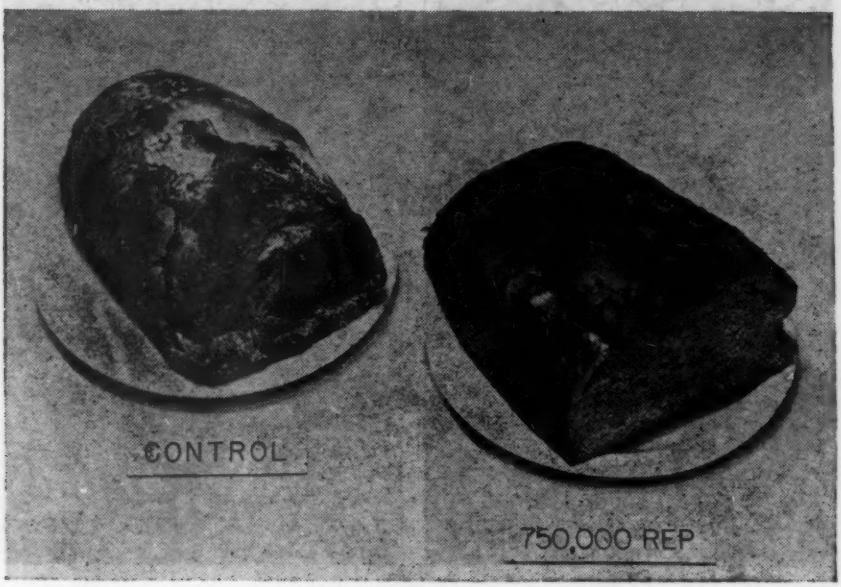


EXHIBIT 242. Hearth rolls, 4 months room temperature (gamma).

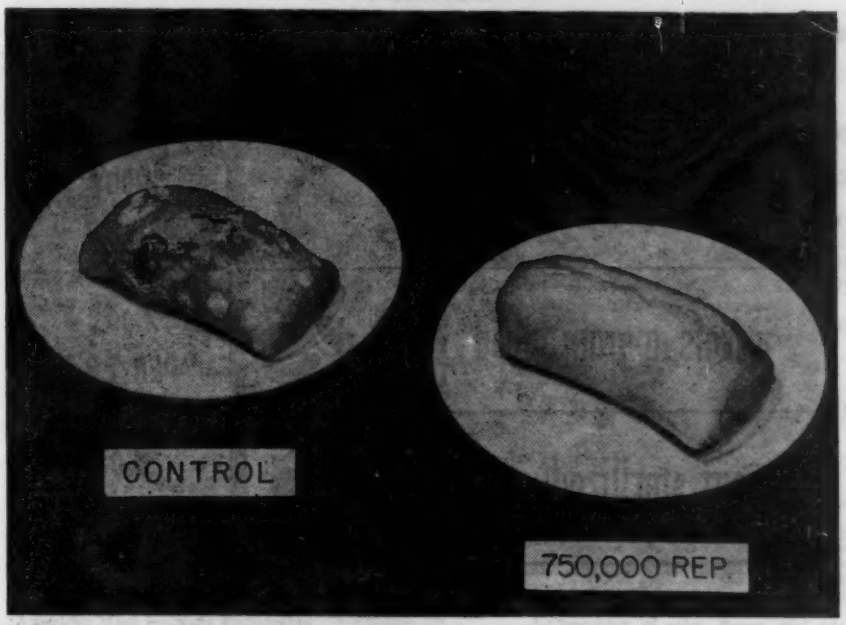


EXHIBIT 243. American cheese, 3 months, room temperature (mold inhibition).

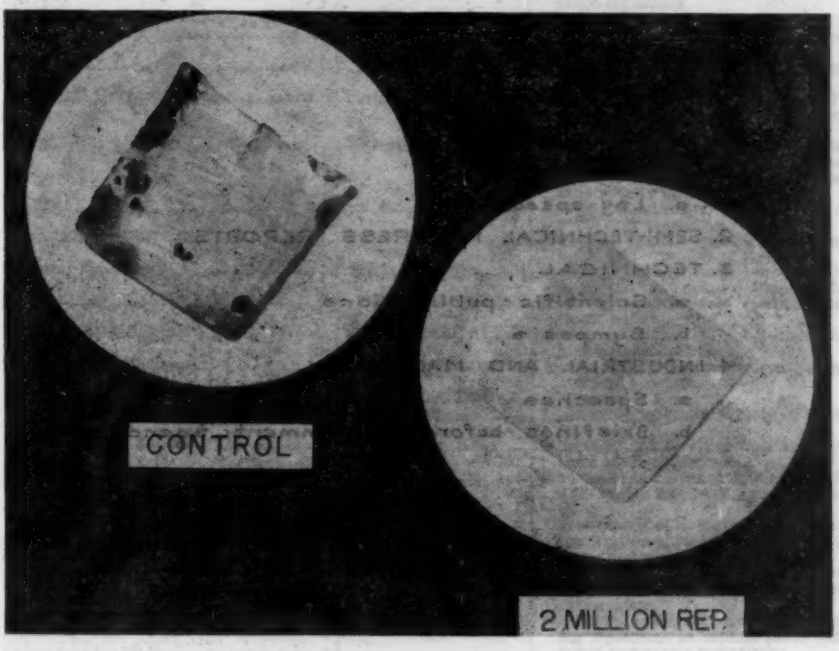


EXHIBIT 244

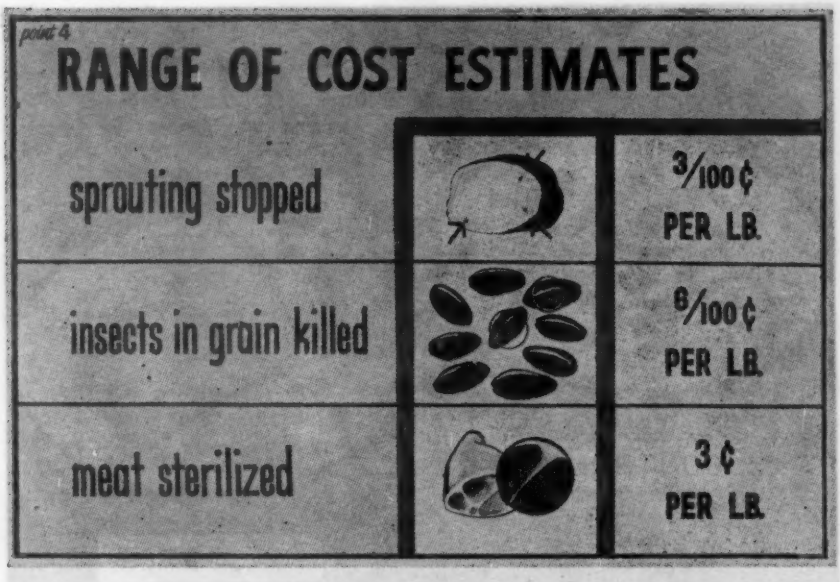


EXHIBIT 245

POPULAR RELEASES

1. POPULAR RELEASES
   a. Press
   b. Radio
   c. Television
   d. Exhibits
   e. Lay speeches
2. SEMI-TECHNICAL PROGRESS REPORTS
3. TECHNICAL
   a. Scientific publications
   b. Symposia
4. INDUSTRIAL AND MANAGERIAL
   a. Speeches
   b. Briefings before Government agencies

EXHIBIT 246

Publications on radiation preservation of food available from U. S. Department of Commerce

		Publication
PB 111636S	Bibliography on Ionizing Radiations, Supplements No. I and II	$11.00
PB 111637S	Subject Index on Ionizing Radiations, Supplements No. I and II	4.25
PB 111634	Radiation Sterilization—Review of Literature in Selected Fields	2.00
PB 111635	Bibliography on Ionizing Radiations—Part I	6.75
PB 111636	Bibliography on Ionizing Radiations—Part II	8.00
PB 111637	Subject Index on Ionizing Radiations—Part III	7.25
PB 121103	U. S. Army Panel Discussion on Radiation Preservation of Food	.50

EXHIBIT 247

Department of the Army research contracts on the radiation preservation of food, May 22, 1956

Organization	City and State	Title
Alabama Polytechnic Institute [1]	Auburn, Ala	To study the nutritive value and long-range effects of irradiated foods in animals with special reference to the chemical and nutrition changes in vitamin cholines and related nutrients.
American Meat Institute Foundation	Chicago, Ill	Chemistry of color, flavor, and odor changes in irradiating meat.
Do	do	Radiation sensitivity of meat spoilage micro-organisms.
Armour Research Foundation of Illinois	do	Irradiation of lipid protein systems.
Columbia University [1]	New York, N. Y	To conduct studies on nutritive and biochemical effects of radiation.
Do	do	Biochemical activity in radiation sterilized materials.
Columbia University	do	Effects of ionizing radiation on the development of off-odor and flavor in protein.
Cornell University [1]	Ithaca, N. Y	Effect of ionizing radiation on the nutritive value of foods as determined by growth reduction for lactation study with dogs.
Do	do	Effects of radiations on structure of fruits and vegetables.
Florida State University	Tallahassee, Fla	Effect of gamma radiation on odor, color, and vitamins of meat.
General Electric Co	Milwaukee, Wis	Study of chemical changes produced in irradiated proteins and amino acids.
Do	do	Loan of 1-million-volt electron generator with operator.
Hormel Institute (University of Minnesota).	Austin, Minn	Changes produced in lipid materials by high-energy radiations.
High Voltage Engineering Co	Cambridge, Mass	Rental agreement for electron accelerator and operator.
Howard University	Washington, D. C	Chemistry of taste.
Iowa Agriculture Experiment Station	Ames, Iowa	Chemical changes in protein of sterilized meat.
Johns Hopkins University [1]	Baltimore, Md	Effects of high levels of ionizing radiations on animal tissues.
Laboratory of Vitamin Technology, Inc	Chicago, Ill	The use of additives in eliminating the undesirable effects of ionizing radiations.
Massachusetts Institute of Technology	Cambridge, Mass	Development of a method of radiation sterilization of foods without adverse flavor and chemical changes.
Midwest Research Institute	Kansas City, Mo	Study of chemical additives for foods to prevent damage during radiation preservation.
National Canners Association	Washington, D. C	Study of the destruction of food poisoning organisms in canned foods subjected to ionizing radiations.
North American Aviation, Inc	Los Angeles, Calif	Logistic and economic feasibility study on radiation sterilization of food.
Ohio State University Research Foundation.	Columbus, Ohio	Chemical and organolempic changes in carbohydrates and proteins produced by radiation sterilization.

See footnote at end of table.

EXHIBIT 247—continued

Department of the Army research contracts on the radiation preservation of food, May 22, 1956—continued

Organization	City and State	Title
Oregon State College [1]	Corvallis, Oreg	Short- and long-term survival and breeding capacity of rats fed high levels of food stuffs sterilized by ionizing radiation.
Do	do	A correlation in radiation sterilized foods of the chemical changes associated with the characteristic flavor development.
Do	do	Flavors of foods sterilized by combining conventional processing with ionizing radiations.
Do	do	Increasing the acceptance of irradiated meat and meat products by selected treatment before, during, and following irradiation.
Pennsylvania State University	University Park, Pa	Odor and flavor problems in radiation sterilization of foods.
Southern Research Institute	Birmingham, Ala	Study of flavor and chemical changes in food during sterilization by radiation.
Southwest Research Institute	San Antonio, Tex	Detection of radiation induced free radicals by paramagnetic resonance.
Stanford Research Institute	Menlo Park, Calif	Flavor changes induced by radiation sterilization.
Do	do	Comparative study of the effects of high and low intensity in radiation in food sterilization.
Do	do	Irradiation services.
Syracuse University	Syracuse, N. Y	The chemical enhancement of bacterial radiosensitivity in the radiation sterilization of foods.
Texas Agriculture Experiment [1] Station (Texas A. and M.)	College Station, Tex	Long-range investigations of the nutritive properties or irradiated foods.
USDA (for work at Agricultural Marketing Service).	Beltsville, Md	Control of postharvest diseases of fruits and vegetables by radiation treatment.
U. S. Testing C., Inc	Hoboken, N. J	Psychometric evaluation of selected irradiated food items.
University of California [1]	Los Angeles, Calif	To study the mechanism extent and means of prevention of the impairment of the safety and nutritive value of foodstuffs resulting from the initiation of a damaging chain reaction by exposure of essential unsatisfactory fatty acids in foods to the ionizing radiation required for the sterilization of foods.
University of California, food technology department.	Berkeley, Calif	Effects of ionizing radiations on carotenoid stability.
University of California	do	Relationships of radiation induced fat oxidation and flavor, color, and vitamin changes in meat.
Do	do	Effects of ionizing radiations on the nutritive and safety characteristics of foodstuffs.
University of Chicago	Chicago, Ill	Effects of irradiation on Cl. botulinum toxin subjected to ultracentrigufation.
University of Colorado [1]	Boulder, Colo	The nutritional adequacy and probable toxicity of foods sterilized by ionizing radiation.
University of Illinois [1]	Urbana, Ill	To study the biological value of the protein of foods sterilized by irradiation as compared to the biological value of the protein of foods conventionally sterilized.
Do	do	Isolation and identification of the stale flavor components which develop in whole dry milk (as a result of irradiation).
University of Illinois, board of trustees	do	Studies on radiation sterilization of sliced apples.
University of Massachusetts	Amherst, Mass	Effects of irradiation on pigmented foods used in rations for the Armed Forces.

See footnote at end of table.

EXHIBIT 247—continued

Department of the Army research contracts on the radiation preservation of food, May 22, 1956—continued

Organization	City and State	Title
University of Michigan [1]	Ann Arbor, Mich.	Chick feeding studies using gamma irradiated food.
Do	do	Combined effects of heat and radiation in food sterilization.
Do	do	Gamma ray sprout inhibition of potatoes.
Do	do	Use of combined heat and radiation for sterilization of foods.
University of Rochester [1]	Rochester, N. Y.	The effect of ionizing radiation on the digestion and protein of fat in vivo.
University of Wisconsin	Madison, Wis.	Inhibition of enzymatic activity in irradiated foodstuff.
Utah State Agriculture Experiment Station.	Logan, Utah	Studies on radiation pasteurization on radiation sterilization of fruit and vegetable products.
Wisconsin Alumni Research Foundation. [1]	Madison, Wis.	The possible carcinogencity of irradiated foods.
Do. [1]	do	Using animal feeding studies on wholesomeness of irradiated foods.

[1] Surgeon General contracts.

EXHIBIT 248

INDUSTRIAL COOPERATIVE AGREEMENTS

1955:
- American Can Co.
- National Canners Association
- Pillsbury Mills
- Swift & Co.

1956:
- American Can Co.
- American Crystal Sugar Co.
- AMF, Atomics, Inc.
  - Bangor & Aroostook Railroad
  - Arrowhead Production Co.
  - Idaho Potato Processors Association
  - J. R. Simplot Co.
  - Miller Pre-Pared Potato Co.
  - Tater State Frozen Food
  - H. C. Baxter & Bros.
- Anaheim Cold Storage Co.
- Armour & Co.
- Basic Vegetable Products, Inc.
- Continental Can Co.
- Doughnut Corporation of America
- Hormel & Co.
- McCormick & Co.
  - Esskay Packing Co.
- Pepperidge Farms
- Pillsbury Mills
- Quaker Oats
- Swift & Co.

EXHIBIT 249

MEMBERSHIP OF THE INTERDEPARTMENTAL COMMITTEE ON RADIATION PRESERVATION OF FOOD

Chairman: Mr. William H. Martin, Director of Research and Development, Office of the Secretary of the Army. Code 131, extension 56153, room 3E394, the Pentagon.

Executive Secretary: Dr. R. G. H. Siu, Technical Director, Quartermaster Research and Development. Code 131, extension 74862, room 2025, temporary A building.

Department of State

Member: Mr. Girard Smith, Special Assistant to the Secretary for Atomic Energy. Code 191, extension 2464, room 7258, New State Building.

Alternate: Mr. George Spiegel. Code 191, extension 4418, room 7258, New State Building.

Department of Agriculture

Member: Mr. Ervin L. Peterson, Assistant Secretary of Agriculture. Code 161, extension 3306, room 219, Administration Building.

Alternate: Dr. George Irving. Code 161, extension 5213, room 302, Administration Building.

Department of Commerce

Member: Mr. Charles F. Honeywell, Administrator, Business and Defense Services Administration. Code 164, extension 4913, room 4846, Department of Commerce Building.

Alternate: Mr. Jacob M. Schaffer. Code 164, extension 4365, room 4064, Department of Commerce Building.

Department of Health, Education, and Welfare

Member: Dr. Lowell T. Coggeshall, Special Assistant to the Secretary for Health and Medical Affairs. Code 176, extension 4254, room 5238, Health, Education, and Welfare Building.

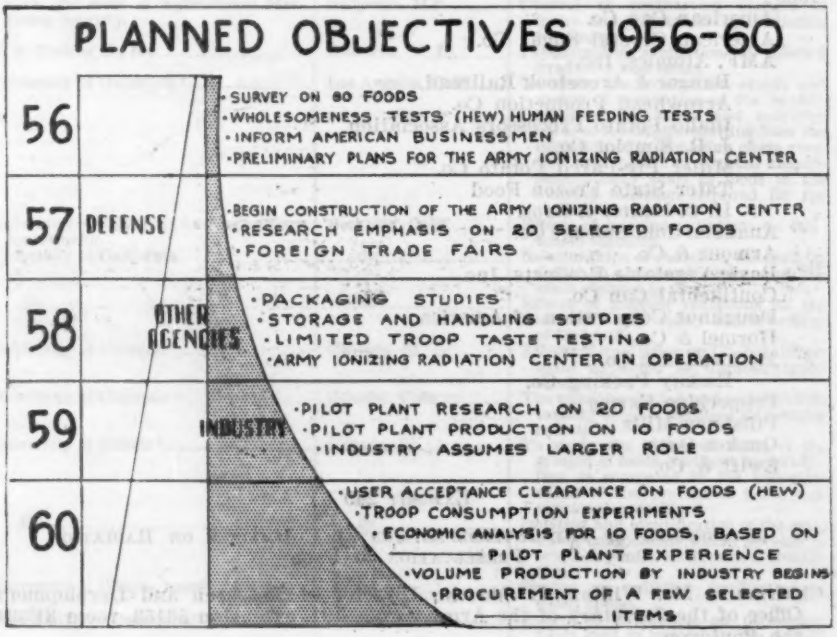
Alternate: Mr. George P. Larrick. Code 176, extension 5140, room 3360, Health, Education, and Welfare Building.

The Atomic Energy Commission

Member: Mr. A. Tammaro, Assistant General Manager for Research and Industrial Development. Code 144, extension 401, room 354, 1901 Constitution Avenue.

Alternate: Dr. Charles Dunham. Code 144, extension 208, room 1013–A, 1717 H Street NW.

EXHIBIT 250



Colonel JACKSON. Now one of the points is: Are irradiated foods tasty?

As you recall from last year's discussion, the reaction of foods to radiation carries from food to food. During the past year we have surveyed over 80 foods. Quite a few of the irradiated foods show considerable promise. Typical of these are pork loin and pork sausage. The former has been demonstrated to show no noticeable change in appearance and taste after 9 months storage at room temperature.

In exhibit 235 we have some photographs that show both roast pork and roast beef which have been stored for 5 weeks at room temperature and then roasted.

Representative COLE. Colonel Jackson, I understand there is a person in the room who has actually consumed pork which has been irradiated. I wonder if he would mind telling us about the appearance and taste and reaction. I leave it entirely up to him if he is listening. He is doing an awful lot of walking around the room. If he wants to tell us about it, I would like to hear him.

Colonel JACKSON. I see you are referring to Dr. Siu. There are several in the room.

Representative COLE. I thought he was the only person. I did not want to identify him unless he wanted to be identified.

Dr. SIU. We, quite a few of us, tasted pork——

Representative COLE. Tasted what? I cannot hear you.

Dr. SIU. Pork which had been irradiated and stored for at least several months at room temperature. I was not able to tell the difference between that piece of pork, after cooking, and any other piece of pork that I have tasted.

Representative COLE. Was the appearance the same?

Dr. SIU. It looked the same to me and tasted the same.

Representative COLE. Colonel Jackson, you indicated that Dr. Siu is not the only one around here. Who else has?

Colonel JACKSON. I have. I have tasted pork, I have tasted beef, I have tasted chicken. I am sure Dr. Bruce Morgan has.

Representative COLE. Anybody else who has done this sort of thing raise your hands.

Colonel JACKSON. Colonel Huber, you have tasted this food?

Colonel HUBER. No, I have not.

Representative COLE. It is indicated there are 6 or 8 in the room at least. Are all of them in agreement in this conclusion there was no distinguishable variance in taste or smell or appearance?

General HASTINGS. On the one item, pork, yes, sir.

Colonel JACKSON. Pork, yes, sir. I think there was quite close agreement in the group that tasted chicken. We had some of our food experts taste some broiled steak.

Representative COLE. Is there any particular reason why the Surgeon General's Office did not participate in this tasting program?

Colonel JACKSON. Well——

Representative COLE. You should not be called upon to answer that.

Colonel JACKSON. They are trying to work out the thing from a very technical standpoint for the protection of the Nation as a whole, and of course they have very technical reasons for doing it. I am sure that the tasting has been done by a great many people.

Representative COLE. I am curious on this irradiated pork.

Colonel JACKSON. Yes, sir.

Representative COLE. Is it necessary to cook it, roast it, fry it, and broil it as long as, for the same length of time that we do pork that has not been treated to gamma rays?

Colonel JACKSON. I would say, as a general rule, it is the same.

Representative COLE. You have to cook it the same length of time?

Colonel JACKSON. However, there is a tenderizing effect in some meats from irradiation due to a difference in the enzymatic action which takes place.

Representative COLE. Can we look forward to the time when we can enjoy a rare pork chop with the same pleasure that we enjoy a rare tenderloin?

Colonel JACKSON. Yes, sir. You can irradiate pork and kill the trichina. That is very definitely true. It has been proved. We have not done it on a commercial scale. It is certainly possible. As such, trichina can probably be eliminated as a hazard to man, really, if this process is extended to that place where pork is consumed.

Representative COLE. Have you had a rare pork chop? Have you eaten one?

Colonel JACKSON. No, sir; I have not.

Representative COLE. Have you, Dr. Siu?

Dr. SIU. No, sir. I will try one before the next hearing.

Colonel JACKSON. I will be glad to try one.

Representative COLE. When you do let me know how it tastes. I would like to try it myself.

Colonel JACKSON. I will.

Representative COLE. All right.

Colonel JACKSON. On the next picture there is bacon, which has some remarkable features. Irradiated sliced bacon with a salt content comparable to the civilian product, rather than the high salt content now used in Army bacon, shows good taste acceptance after 6 months at room temperature. This same product in frozen storage, has remained satisfactory three times as long as the frozen nonirradiated bacon, which is our current method of shipping overseas. That is an important point.

Representative COLE. What is the meaning of the word "control"?

Colonel JACKSON. "Control" is not irradiated. It is the product in its natural state prior to irradiation. That is, we start out with two samples. We take one and irradiate it and the other one we keep the same and see what happens.

Representative COLE. On bacon you have three, probably with varying degrees of radiation.

Colonel JACKSON. In the particular picture, these products were frozen, so the control was frozen. It would be very similar to what you would get from frozen bacon. Then this picture is taken after it has thawed out. The two samples of 3 million "rep" and 6 million "rep" show much better appearance and did not have a color change. What we are trying to show here is the advantages of this process over food-handling methods currently in use.

Representative VAN ZANDT. Colonel, after the food has been removed from either the plastic bag or a can, how long does the housewife have before that food will spoil?

Colonel JACKSON. I would say, although we have not run any particular experiments on it, the answer to that will be that food that

has been irradiated will keep as long as you keep it from becoming contaminated. As soon as you remove the container and the air is free to contaminate it, it will react the same as any other food of the same type as it is today. Exactly the same.

Representative VAN ZANDT. In other words, it is subject to the same treatment as the food you buy today in the corner grocery store?

Colonel JACKSON. Yes, sir. As long as you keep it from being contaminated it will last a long time, but the minute you open and expose it to bacteria it will go just like food goes that has not been irradiated.

Representative VAN ZANDT. If the housewife freezes it immediately or places it in the refrigerator, will that extend the life?

Colonel JACKSON. Yes, sir, refrigeration definitely. In fact, we have run various experiments, with some foodstuffs after irradiation and refrigeration. We have extended the shelf life as many as five times its value without irradiation, which is quite significant.

Representative COLE. Are you going to discuss each one of these specimens in your statement?

Colonel JACKSON. Yes, sir.

These photographs (exhibit 237) show the samples of chicken, poultry. Poultry results actually have been very encouraging, and we have experimented upon both fresh and precooked irradiated chicken, which, stored for 4 months at room temperature, resulted in a highly accepted product. In these pictures, you will notice the precooked sample one, semicooked, on the right prior to irradiation, and the one on the left was an uncooked chicken. The precooked chicken was not completely cooked but partially cooked, and the other one on the left was not cooked.

Representative VAN ZANDT. Prior to irradiation?

Colonel JACKSON. Prior to irradiation. And you see that there is quite a difference in the final appearance of the chickens when they are finally cooked ready to eat.

We have some exhibits right here with which I can illustrate that point. This chicken was irradiated March 19, 1956, to 2.5 million "reps" of gamma rays and stored at room temperature.

This chicken was irradiated partially precooked on March 19 at 2.5 million gamma rays and has been stored at room temperature in a container. We have taken it out of the container.

This is a chicken that was irradiated fresh on March 19, 1956. Then it has been stored at room temperature, and it was roasted today.

Representative COLE. This first one [indicating]?

Colonel JACKSON. Yes, sir.

Representative COLE. It was irradiated at the same time as the one cooked today—the first and third ones?

Colonel JACKSON. Yes, sir. It was irradiated in March.

Representative COLE. At the same time as the first one?

Colonel JACKSON. That is correct.

Representative COLE. And in the same amount?

Colonel JACKSON. That is right.

This squab was irradiated on March 19, 1956, at 2.5 million "reps" and stored at room temperature. It was roasted today. This second squab here was irradiated and partially precooked. This one was not cooked. You can see the appearance. Actually what we are looking for is the best looking product in poultry for our use. Squabs are

a good experimental fowl. We do not use squabs in the Army. But chickens and turkey——

Representative COLE. You spoke up awfully fast on that one, Colonel.

Representative VAN ZANDT. For the benefit of the record, what do you mean when you say "rep"?

Colonel JACKSON. A "rep" is roentgen equivalent physical, and it is a term utilized by the physicists to designate really a unit of radiation energy.

Representative VAN ZANDT. It is a measurement?

Colonel JACKSON. A measurement, sir, of the energy that the material has absorbed. If it has been irradiated 2.5 million "reps" it has absorbed that much.

Representative VAN ZANDT. I notice that 2.5 million "reps" were applied to the chicken in front of you.

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. How long did it take? What amount of exposure from the standpoint of time?

Colonel JACKSON. I think I would have to call on Dr. Morgan to answer that.

Dr. MORGAN. Approximately 15 minutes.

Colonel JACKSON. How many?

Dr. MORGAN. Fifteen minutes.

Representative VAN ZANDT. Were you using waste material?

Dr. MORGAN. We were using waste reactor fuel from Arco, Idaho materials testing reactor.

Representative VAN ZANDT. If you had a piece of fresh material, would it cut down the 15-minute time?

Dr. MORGAN. It would, sir. We are using this time interval at the present time as a research tool. If we had more recent products from the reactor, our time would be shorter.

Representative VAN ZANDT. Could you give us some estimate of the time element if you used a piece of fresh material?

Dr. MORGAN. We desire to have a holding time of the food in the area where it has been treated of approximately five minutes. That would appear to be desirable at the present time.

Representative VAN ZANDT. Then your ultimate objective is 5 minutes?

Dr. MORGAN. Yes, sir.

Representative VAN ZANDT. At the present time it takes 15 minutes?

Dr. MORGAN. This is our best time, 15 mintues.

Representative VAN ZANDT. The staff member just mentioned a very important item that should be in the record. When you get your research reactor you can take the energy right from that reactor?

Dr. MORGAN. That is what we conceive; yes, sir.

Representative VAN ZANDT. That will cut down the time considerably.

Dr. MORGAN. It will.

Colonel JACKSON. Studies on fish products have been expanded. In our brochure on the next page (exhibit 238(it shows some oysters. Shrimp and oysters have shown considerable promise. The brochure picture demonstrates samples of oysters after 5 weeks' storage at 70° F. In both methods of preparation, the product was found to be

tasty. This is a product without counterpart on today's markets. We must refrigerate oysters.

Representative VAN ZANDT. You have been feeding the class at Fitzsimons Army Hospital haddock, have you not?

Colonel JACKSON. Yes, sir. Shrimp and oysters are the two new foods in this last fiscal year that we think show additional promise. This is in addition to what we had told you previously.

Pasteurizing doses of radiation using strawberries and grapes prolonged their storage by a factor of three in experiments designed to duplicate distribution cycle temperatures. By that we mean normally in the handling of strawberries you refrigerate them part of the way in transit, and then they sit in a store normally not refrigerated. We tried to compare that method of distribution and see if irradiation would assist in the keeping qualities of the strawberries, and it definitely did. It increased their life, we will say—normally strawberries must be marketed in about 3 days. These would last about 9 days.

Representative VAN ZANDT. What about the color?

Colonel JACKSON. At the dosages used the color was satisfactory.

Representative VAN ZANDT. Is that true of both the strawberries and the grapes?

Colonel JACKSON. At higher dosages the red of the strawberry does definitely bleach out.

Representative VAN ZANDT. How about the grapes?

Colonel JACKSON. The grapes I did not see. Dr. Morgan can answer that.

Dr. MORGAN. The color was satisfactory; yes, sir.

Representative COLE. What is the experience with dairy products?

Colonel JACKSON. In dairy products, we have run certain experiments with milk, raw milk, raw skim milk, and milk powder, and then cheese. We have found that they normally produce an off-flavor by irradiation. That is, irradiation at the dosages necessary to sterilize does produce an off-flavor.

We are working on it to find what it is that happens, to see what we can do to correct that. We do not know the answer at this time.

Representative COLE. Is the off-flavor any more pronounced with respect to cheese than it is with milk?

Colonel JACKSON. No, sir. In fact, various cheeses react differently. Some of them become very bland. Some of them take on a flavor similar to what we buy in cheese—smoky flavor. There is no one particular characteristic flavor. The cheese loses its normal acid flavor you associate with cheese. It is a different flavor, and all of this flavor—actually we are talking about different flavors, and there is no real base line to say what is outside of what we normally use today.

Of course, in the food industry various processes change the flavors of food. Although the taste from irradiated foods is different, the taste panels have found in many cases it is not an undesirable flavor. It is different. In some cases, however, there are flavors that are what you would not care to eat at the present time. But that is not true of all.

Representative VAN ZANDT. What has been your experience with powdered milk?

Colonel JACKSON. Dr. Morgan, can you answer that question?

Dr. MORGAN. We have taken powdered milk, both whole and fat-free, and irradiated it. In both cases we got an objectionable product. The degree of difference was evident between the two. We felt there might be a reaction specifically with the fat.

Representative VAN ZANDT. Thank you, Dr. Morgan.

Colonel Jackson, your next subject is string beans and so forth; is that correct?

Colonel JACKSON. Yes, sir.

Green beans have shown good promise in some of the more recent experiments. That is in addition to some of the other vegetables that we discussed last year. We had quite a long list of them. Green beans are one of the more favorable ones we have added this year.

Representative VAN ZANDT. As I recall, last year you reported that several types of vegetables collapsed under the bombardment. Have you had any additional experiences which you could report at this time?

Colonel JACKSON. The destruction of the texture by irradiation is actually in direct ratio with the dose level that you apply. What we are trying to do is find ways of accomplishing what we want with the minimum dose level we can get.

By various packaging means and treatments, we have found various ways of reducing the high dosage required. These chickens have been subjected to 2.5 million reps. That is a tremendous amount of energy actually, and if we can reduce it, it is highly desirable.

Representative VAN ZANDT. What about tomatoes?

Colonel JACKSON. We have not been able to sterilize tomatoes without breaking the texture down. They do leak, and we have not tried to—no doubt you can inhibit mold of fresh tomatoes, but you would have to package them in some type of flexible package. We have not gone into that. We have run some experiments on trying to sterilize them and the texture does break down.

Representative VAN ZANDT. Does it apply also to lettuce and celery?

Colonel JACKSON. Every one reacts a little bit differently. Lettuce, definitely the structure is broken down at high energy levels. However, we think it is within the realm of possibility to extend the shelf life of lettuce under refrigeration by radiation, where you would irradiate only at lower dosages. That would inhibit the formation of certain types of mold.

Representative VAN ZANDT. What experience have you had with fruits? I am thinking of apples, peaches, and so forth.

Colonel JACKSON. Maybe I had better not try to answer that. I think Dr. Morgan can answer the one on apples.

Dr. MORGAN. We have irradiated apples under various normal conditions, such as in the presence of vitamin C, which is the normal technique of apple preservation, keeping them at different times after harvest and different terms, and we have found we can produce an apple commodity which might be used in apple pie, for instance, either with or without the condiments that might be added. This product has stood up at the present time for 3 months, at latest reading, at room temperature. When it comes out it is not browned as an apple normally would be browned, but would be light.

Representative VAN ZANDT. I am going to ask this question for my colleague from California, Carl Hinshaw. What experience have you had in irradiating fresh lemons?

Colonel JACKSON. Dr. Morgan also can answer that. Lemons and oranges. We have tried both citrus products.

Dr. MORGAN. We have used the approach that we are trying to get rid of the blue mold that normally occurs on the surface of the skin, both with an industrial group and under a contractual arrangement. We have two groups studying this, and the results in general are that you can extend the shelf life of lemons or prevent this mold. There is some texture loss. The end point between extending the shelf life and the texture loss is a very sensitive point, but I think we can extend the shelf life without a great loss in texture.

Representative VAN ZANDT. Do you have any comment Dr. Siu?

Dr. SIU. That is the comment I would have made, sir.

Representative VAN ZANDT. Thank you. Go ahead, Colonel.

Colonel JACKSON. Irradiated flour remained insect free after 9 months of storage temperatures up to 100° F., and when properly packaged and when used in baking bread produced loaves of bread with normal characteristics. The next photograph (exhibit 240) in this brochure is shown some samples, that is, slices of bread made from flour that has been irradiated under various energy levels, and then stored at 9 months at 100° F.

The first picture on the left is the control. You will notice on the side there are two moisture levels of flour, of the bread in each case, and then 50,000 reps and 275,000 reps and 475,000 reps. Then the lower part of the picture, it is stored at 40° F. of normal refrigeration chill temperatures. You notice the texture is very good. The bread rose properly. The glutin formed properly.

Representative VAN ZANDT. Have you retained the color, Colonel?

Colonel JACKSON. The color is good at these levels.

Representative VAN ZANDT. The control piece of bread retains 12.1 percent of its moisture. Is that right?

Colonel JACKSON. No. All of these are 12.1. They go across this way [indicating]. The moisture is not changed by irradiation.

Representative VAN ZANDT. It is not?

Colonel JACKSON. No, sir. Actually this is a recap of 4 different experiments in 1 photograph.

The last point on this chart is: Is the irradiation process economical?

At the hearing last year, preliminary estimates of various workers in the field were mentioned. The current estimates are shown in brochure exhibit 244, and on the next chart we have our best estimates as they are today. To inhibit the sprouting of tubers such as potatoes, the estimate is still .03 cent per pound.

To kill insects in grain such as wheat or flour, .06 cent per pound.

Now to sterilize meats, our best estimate today is 3 cents per pound.

Those are averages between certain broad estimates. In fact it has been reported that maybe it would cost as high as 7 cents, but we think 3 cents is a good average price that we think we are capable of meeting.

Representative VAN ZANDT. If my memory serves me correctly, I think you quoted $4 a ton last year for potatoes.

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. If my figure is correct, you have made a great reduction in the cost.

Colonel JACKSON. Yes, sir. The $4 a ton was an estimate by someone in the industry, based on their studies. I do not recall who it was.

But these are some of the better estimates we are getting from industry and based on our experience.

Representative VAN ZANDT. Would the sterilizing cost of 3 cents a pound apply to pork?

Colonel JACKSON. Yes, sir. That is a sterilizing dose of 2.5 million reps just like we had there, which takes about 15 minutes for the piece of meat.

Representative VAN ZANDT. Did you quote 29 cents a pound last year?

Colonel JACKSON. Seven cents.

Representative VAN ZANDT. You made a reduction there.

Colonel JACKSON. We think it is coming down. We think it will come down still lower. But the only way we feel we will ever get it is to really make some in large quantities, and that is the purpose of our pilot plant.

Representative COLE. Colonel, on the question of cost, what is the estimate of saving to the Quartermaster General's office if perishable foods could be preserved by irradiation and not require refrigeration?

Colonel JACKSON. Various studies have been made.

We do not think that radiation will completely eliminate refrigeration from the Quartermaster Corps. We do think that there are many applications where we can substantially reduce it or eliminate it in certain areas. We do not think this process will do away with all refrigeration.

Representative COLE. I would like to have a statement from Dr. Siu, who one time indicated to me in an informal conversation the savings that could be realized by the military services if all of its food requirements could be preserved by radiation. It is a fantastic figure. Doctor, be as nearly accurate as you can.

Dr. SIU. If you prefer a confirmed calculated figure, we can go back and calculate and give you the figure. If you want a personal estimate——

Representative COLE. Yes.

Dr. SIU. I would say tens of dollars per man per year overseas.

Representative COLE. You would say what?

Dr. SIU. Tens of dollars per man per year overseas. For 1 million men overseas it would be in the tens of millions of dollars per year. During World War II we had about 5 million men overseas. So it would be——

Representative COLE. You are saying it would represent the saving of $10 per man?

Dr. SIU. Tens of dollars, and exactly where, 10 or 20 or 30 or 40, et cetera, is dependent upon how you approach the estimate, whether you amortize the merchant marine costs and so forth.

Representative COLE. Then it would represent a saving of from $10 to $50 per person in the service?

Dr. SIU. That would be overseas.

Representative VAN ZANDT. What is the annual food bill for the Military Establishment?

General HASTINGS. For the Department of Defense it approaches $1 billion a year.

Representative VAN ZANDT. One billion?

General HASTINGS. Yes, sir.

Representative VAN ZANDT. Have you any idea of the costs of transportation of food both on a dry and on a refrigerated basis?

General HASTINGS. I do not have that here, sir.

Representative VAN ZANDT. Could you supply such information for the record at this point?

General HASTINGS. Yes, sir.

Colonel JACKSON. We can give you those figures. We did not bring them with us. I think we gave them at one of the closed sessions, and it is our fault we did not bring them with us today.

(The information referred to follows:)

Comparable costs per pound (laid down destination), perishables versus nonperishables

(Origin point in United States—Chicago, Ill.)

	Perishables	Nonperishable	Differential
Europe (Giesen, Germany) commercial	$0.0523	$0.0351	$0.0172
Japan (Tokyo, Japan) commercial	.0701	.0494	.0207

NOTE.—Published tariff rates for continental United States rail transportation and commercial shipping rates for the specific products included in the perishable portion of the subsistence ration, including port handling costs paid by the military on an average basis.

ESTIMATES OF PRINCIPAL MILITARY ADVANTAGES THAT WILL ACCRUE UPON SUCCESSFUL COMPLETION OF RADIATION PRESERVATION OF FOODS PROGRAM

1. The minimization of refrigeration in the battlefield will be a significant contribution to the Army's mobile forces. A reduction in the logistical load is vital to the Army's need for mobility, flexibility, and dispersibility. All military services will benefit immeasurably by the elimination or reduction of freezer and refrigerated storage and transportation facilities. Nuclear submarines, for example, will not require precious space for refrigerated storage; more time can be spent at sea since food-replenishment stops will be less frequent. For Air Force long-range missions, refrigerated foods will not be required.

2. The amount of fresh foods in the combat man's diet can be significantly increased; this will be especially important in sustaining the fighting man's morale under austere conditions.

3. Refrigeration reduction, with attendant reductions in operational and maintenance support, will release additional manpower for combat duties.

4. In addition to the primary military advantages, the radiation preservation of food program will result in a savings in dollars. Although precise values are not available until production costs are known, a rough estimate, involving one military situation (which includes consideration of transportation, storage, spoilage, equipment, operation, and making adjustments for cost of irradiation and packaging) indicates a potential savings of approximately $40 per man per year overseas.

Representative COLE. You have made such studies?

Colonel JACKSON. We have made some studies; yes, sir.

Representative COLE. If you have not, I think it would be very important that you do make rather carefully contemplated studies to see to what extent successful preservation of food by irradiation can reduce the costs of preserving, storing food used by the military services.

Colonel JACKSON. Yes, sir.

There is one added feature, too, that we look upon very importantly. That is, we feel that this method will permit us to serve what is today a very perishable item to troops in combat that you cannot do today. You cannot get refrigeration there. You cannot get a refrigerated

product there. We think that is a very important factor in any future war where you have this mobility that you must have in the armies of the future, extreme mobility. You will not be able to carry refrigeration around with you and worry about refrigeration. To give the soldier the very best food, we think this process has great capabilities of giving us this additional potential in addition to what any comparison you could make on dollars and cents on past experience.

Representative COLE. It is my feeling that food preservation offers the most promising, glowing, happy prospect for the peaceful use of atomic energy of any of the others to the various peoples throughout the whole world. So I am very anxious for you folks to get along with your program just as fast as you can, both by way of proving that the irradiated foods are not harmful——

Colonel JACKSON. Yes, sir.

Representative COLE. And by way of showing how cheaply they can be irradiated.

Colonel JACKSON. Yes, sir; we certainly thank you, because it is most encouraging to have your support, sir. We certainly have profited by it very much, and we are looking forward to a very rapid program within the limits of our capabilities.

Representative VAN ZANDT. Colonel, when you furnish for the record the information on the cost, I hope that you will take into consideration various factors such as the cost of radiation, the cost of packaging, and so forth.

Colonel JACKSON. Yes, sir; this estimate we have discussed here, we think, can only be confirmed by a plant, and our preliminary plans for the establishment of our Army ionizing radiation center are coming along quite well. This center will consist of three main parts: A gamma ray producing reactor to be designed and built by the Atomic Energy Commission, a linear accelerator to be designed and built under contract, and a food-processing pilot plant. The work is progressing according to the schedule we discussed with you last year. We have every indication that the pilot plant will be operating in the latter part of 1958. In addition, an economic feasibility study by a very large industrial firm is in progress, and they will develop additional information which will be useful in determining prospective cost figures.

Summarizing this section of the presentation, we can say that the technical risk has been reduced considerably during the past year. The promise looks brighter than ever. I am not suggesting by such optimism that all the technical problems, or even the principal ones, have been solved. On the contrary, there is a long way to go. As a matter of fact, as research mounts into the pilot-plant stage, a new dimension of problems with increasing costs unfolds.

Now let us turn to a discussion of what action we are taking to transfer to and encourage civilian industry and get this into the free economy as rapidly as possible. During the past year, we have taken determined steps with encouraging results. We have effected a wide distribution of information. We have broadened the base of knowledge. We have markedly increased the degree of active industrial participation. And we have established a formal means of Federal interdepartmental collaboration.

RELEASE OF INFORMATION

During the past year the progress of the program has received nationwide dissemination in press, radio, television, exhibits, and speeches. Over 25 such releases have been made.

Semitechnical progress reports representing the highlights of our technical accomplishments have been distributed to an established industrial mailing list which now consists of over 350 firms. Some 4,000 pieces of literature have been distributed.

The Department of the Army has sponsored open technical sessions before annual meetings of food and allied industries. Since last year we have sponsored or will sponsor programs before the American Chemical Society, Association of Food and Drug Officials of the United States, Institute of Food Technology, Research and Development Associates, Federation of American Society of Experimental Biology. Reports of contractual investigations will be published by the Department of Commerce for release to the public. Brochure exhibit 246 is a list of publications currently available to the public from the Department of Commerce.

The Army is frequently requested to prepare and deliver oral presentations to governmental agencies as well as non-Government groups. We have participated in over 50 technical and industrial programs during the past year.

BROADENING BASE OF KNOWLEDGE

We are continuing to expand the base of knowledge. The majority of our research effort is carried out by means of contracts with universities, industry, and other research groups. Additionally a National Research Council Committee, as well as a Quartermaster Industrial Advisory Committee and the Surgeon General's Advisory Committee on Nutrition, assist us in expanding the base of knowledge in the field. Brochure exhibit 247 lists the institutions supported last year by the Army for research in the radiation preservation of food.

INDUSTRIAL PARTICIPATION

To stimulate industrial interest we devised a system of no-cost-to-the-Government contract with competent industrial organizations on problems of mutual interest. In 1955, four companies particpated. Last year, the number was increased to 22. These organizations are listed in brochure exhibit 248.

INTRAGOVERNMENTAL COLLABORATION

Following a series of briefings to various Government departments last year by an Army team, an Interdepartmental Committee on Radiation Preservation of Food has been formally organized consisting of representation from Departments of State, Defense, Agriculture, Commerce, Health, Education, and Welfare and the Atomic Energy Commission. Membership of this committee is shown in brochure exhibit 249. The committee's functions are:

Provide motivation and broad guidance for the Government research program on the radiation preservation of food.

Effect a transition of program responsibility from the Department of Defense to other Government agencies and to the free economy as rapidly as possible.

Render a semiannual report to the President on the progress made with relation to our Nation's atoms-for-peace effort.

The first meeting was held on May 15, 1956. However, before that meeting, the following governmental agencies were actively contributing to the program:

Atomic Energy Commission: Sources of gamma radiation.

Department of Health, Education, and Welfare: Food testing experimental procedures.

Department of Agriculture: Supplementary studies (microbiological studies on food products).

Department of State: United States Information Agency.

Department of Commerce: Industrial education, and public information.

We can readily see that increasingly intense interest is being generated in the civilian agencies and the free economy. We are looking forward to the day, when this interest reaches the point where the actual commercialization is realized. Given continued strong support from this subcommittee and other legislative and executive leaders, we have every hope that this will arrive within the foreseeable future.

With this quick survey of our progress of the past year, I would like to turn the floor over now to Lt. Col. Truman F. Cook from the Department of Army General Staff. He will describe the Army's plans for the future.

Representative VAN ZANDT. Thank you, Colonel.

Representative COLE. I would like to inquire, as suggested to me by Mr. Brobeck of the staff, nothing has been said with respect to consideration being given by the Army, the Quartermaster, on the preservation of clothing and shoes and boots and such things.

Colonel JACKSON. We have given consideration to that. Not under this project, however. This presentation was entirely confined to food.

Representative COLE. Yes.

Colonel JACKSON. But our research laboratories are working on utilizing this same technique in the preservation of leather and textiles, and they have made some progress. But again they can only make small experiments under presently available——

Representative COLE. I would suppose you could irradiate leather shoes and boots and send them down into the jungles to see what happens to them.

Colonel JACKSON. We have run experiments of this nature, by putting shoes or pieces of leather in plastic bags and sealing them from the air. We have irradiated them. First, we have inoculated the leather, actually, with fungus to make sure it would have spores there, and then we have killed them by irradiation and preserved the shoes. Those experiments are not complete, but we know from those experiments that it is possible to irradiate shoes and ship them to jungles, and as long as the package is not broken they will not mold. That would not prevent—in use you would still have to take care of them. But in storage, which is a very important thing to the Army, where

we are dealing with millions of pairs of shoes during a war, it is totally impossible to go through and get rid of the mold by any other means. This would be a very important factor. We can do it by certain chemicals which may be toxic in high concentrations, and we would like to not use them.

Representative COLE. Another point Mr. Brobeck has raised is the matter of the sterilization problem with the Quartermaster and the Surgeon General as far as sterilizing knives and forks, pots and pans, and skillets. Do you see any prospect of eliminating soap and water and sterilization by steam?

Colonel JACKSON. You are way ahead of us. I will not say any of these things are not within the realm of possibility, but at this point we have done nothing in that.

Representative COLE. It would seem to me it would be very, very remote to get a reactor aboard every ship's mess.

Colonel JACKSON. You would have to find a way of handling nuclear products much simpler than now before you would ever get them in the kitchen or in the household.

Representative VAN ZANDT. Thank you, Colonel Jackson. We will now hear from Lt. Col. Truman Cook.

STATEMENT OF LT. COL. TRUMAN F. COOK, CHIEF, PHYSICAL SCIENCES BRANCH, RESEARCH DIVISION, OFFICE OF THE DEPUTY CHIEF OF STAFF FOR RESEARCH AND DEVELOPMENT, DEPARTMENT OF THE ARMY

Colonel COOK. Mr. Chairman and members of the subcommittee, I would like to summarize our present position regarding future plans.

From an overall analysis of the current state of the art, we believe that the days of excessive technical risk in the program of radiation preservation of food are numbered. There are still large and difficult problems ahead. But we now possess sufficient data to make a reasonable estimate of the success potential. Within a few years the specific areas of practical applications and the profit incentive to proceed should be amply evident to industry.

With this in mind, the Army is proceeding along the following lines:

(*a*) In its present role of spearheading the national effort, the Army will attempt to gradually phase out of the position of dominance. It will rely on the Interdepartmental Committee on Radiation Preservation of Food to stimulate greater participation by other Government agencies and industry to aid in bringing about an effective transition into the free economy. At the same time we will continue to speed up the arrival of this date by increasing the scope of no-cost collaborative arrangements with industrial concerns, by wide dissemination of research data and by spreading the base of know-how by means of research contracts.

Representative COLE. May I interrupt there? Who has decided that the Army is going to phase out of this picture?

Colonel COOK. This decision was arrived at, sir, by realizing that the Army is in the position of the consumer in this program. We also realize for the best interests of the program and also the country this program should be phased——

Representative COLE. I would like to know the arguments that are advanced by the person that came to that conclusion. It appears to me that is just cockeyed. I am disappointed to hear the Army is phasing out of this program. The very fact that the Army is the big consumer is the very reason why it should be in there spearheading this program, because it is the one most interested in seeing it move along and succeed. You move out of the picture, and who is going to care whether it progresses or not?

You cannot answer that, Colonel Cook, I realize. I am just speaking out for the ears or eyes of whoever may hear or read it. But I think it is a great mistake for the Army to abandon or even to move out of the position of spearheading the program.

General Hastings, why is that necessary, that you get out of it? We would not have been anywhere near as far along the road as we are if you had not been in the picture the last 3 or 4 years. Now you come along and tell us you are nicely getting underway and you are going to go into the shadows.

Colonel COOK. I believe I can speak for that, because I have been associated with those that are concerned with the proper policy development of the Government's role in this program, and I have been very close to those people in their discussions and deliberations. I would say it is incorrect to say we are phasing out of the program from a matter of interest point of view. It might be rightfully stated that we are definitely interested in the fast technological progress, and we are very mindful of our responsibility in handling, let us say, the stewardship of this program in such a way that technological progress is not sacrificed.

However, it should be realized the role of the Government, and particularly the role of the Army in a program of this nature, which has tremendous implications in the civil economy, should be such to make our expressions known to other Government agencies which have strong nonmilitary responsibilities in the management, of such a broad program within areas of their concern and interest.

May I illustrate the point by suggesting a few examples?

First of all, we find ourselves in need of good standard dosimeters for measuring radiation in the very high flux range, let us say in the million rep range. This is within the capacity of the Department of Commerce to execute and particuarly the Bureau of Standards. The Bureau of Standards is responsible for the development of standards of measurements which would include radiation standards to be employed by industry and testing laboratories.

We would like to see other Government agencies assume their proportionate share of the program at such a rate that the overall vision and progress of the program is accelerated.

There are strong implications of this program upon the Department of State in promoting the utilization of such a process by foreign countries and in the shipment of our own products to foreign countries.

There are implications certainly in the Department of Commerce in bringing about a rapid transition of this knowledge and this capability to industry.

These things are very definitely in our program. We are unfolding a program of collaborative arrangement and participation within the Government, and we are also strengthening our collaborative arrangements with the industrial and academic life.

Representative COLE. Who is going to take your place when you move out? All you have said, of course, is very nice and understandable. Every Department of the Government should be active and participate in the program and should be interested in it. To be sure. And private industry, commercial enterprises should be participating, collaborating in it. But who is going to supervise the program, spearhead the program, when the Army puts on its armor and moves away? Who is going to do it? Somebody has got to do it if it is done at all.

Colonel COOK. I believe, sir, if you will search you will find certain key individuals who have the program interests at heart and work hard at its proper development. I would like to recognize at this point some of our competent program managers. Dr. Siu, Technical Director to the Quartermaster General, is a stanch supporter and is a very active individual in looking into the proper development of the future of this program. Colonel Jackson, with whom I have daily contact, devotes a considerable portion of his time to the proper execution of the program. Dr. Morgan, project director at the Quartermaster Food and Container Institute for the Armed Forces in Chicago, integrates all of the widely distributed research teams. Lt. Col. Belmont S. Evans, who is in the audience, is assigned to the Army Reactors Branch, Atomic Energy Commission, and to the Office of the Quartermaster General, coordinates the planning on gamma radiation sources including the reactor project. For the food irradiation pilot plant, Col. Tyron Hubes of the Army Surgeon General's Office coordinates the food wholesomeness portion of the program.

Representative COLE. Sure, but when the Army phases out of this program Dr. Siu is going along with the Army and phase out, too. That is what I am worried about. I want to keep him in.

Colonel COOK. May I unfold our program as it is outlined for the future, and then I believe that you will notice that the Army's interest in the program is still vital and will maintain a significant amount of pressure so that the progress is not sacrificed.

I believe what we want is an early realization of commercial development of radiation preserved food, so that the Army can depend upon industry to provide the food that will have to be irradiated. We have to provide sufficient incentive to industry and sufficient information, and we have to cut the risks sufficiently so that industry will move in as rapidly as possible and assume its proper role.

Representative VAN ZANDT. Will the gentleman yield?

Representative COLE. I am all through.

Representative VAN ZANDT. I was going to develop this point a little later on, but I think we should develop it now inasmuch as the gentleman from New York brought it up.

How much money did we spend the first year of this program, in round figures?

Colonel COOK. Approximately $100,000 interest for the Army.

Representative VAN ZANDT. What year did it start?

Colonel COOK. Fiscal 1953 as far as the interest of the Army was concerned.

Representative VAN ZANDT. What is the expenditure for fiscal 1956?

Colonel COOK. Fiscal 1956 was $1,093,000.

Representative VAN ZANDT. How much money was requested for fiscal year 1957?

Colonel Cook. $1,100,000.

Representative Van Zandt. What year do you plan to ask industry to make a contribution to the effort?

Colonel Cook. They are making a contribution today, sir.

Representative Van Zandt. How much?

Colonel Cook. Approximately $500,000 a year.

Representative Van Zandt. What would you ask of them next year?

Colonel Cook. Let's say that we do not ask, sir. We keep track of their interest and the volume of their participation. It is our estimate that their volume of participation by next year will be $1 million.

Representative Van Zandt. What do you estimate for fiscal year 1958 as industry's participation in dollars and cents?

Colonel Cook. We are processing our estimate, sir.

I might review my memory from a chart which we prepared. Again in 1958 we estimate about a million dollars.

Representative Van Zandt. How much will the Government spend in 1958?

Colonel Cook. May I break that down into areas of interest, sir? The Army's expenditures for 1958 will be $1,100,000 for research and development costs; $2,060,000 for plant investment, nonreactor portion of the pilot plant. We do not know at the moment what other Government agencies will spend that year.

Representative Van Zandt. Let me go a little further to conclude this line of questioning. What year do you plan to start reducing the Government's costs and gradually have industry or free enterprise take over?

Colonel Cook. 1959, we will find, is the year of transition, sir. In 1959, the amount of participation by industry should overcome or, let us say, overlap the degree of participation dollarwise by the Government.

Representative Van Zandt. Until the calendar year of 1959, you plan to continue your present program of research and development?

Colonel Cook. That is correct, sir, and beyond.

Representative Van Zandt. Is it your intention to gradually include in the effort the food packers, handlers, and processors of this country?

Colonel Cook. This is our intention, sir; yes, sir.

Representative Van Zandt. By 1959 you feel that you will have completed all of these costly experiments and that free enterprise will have absorbed knowledge to the extent that industry can take over and operate the program?

Colonel Cook. Let's say that the amount of reliable information that will be available at that date will be sufficient, in our opinion, to allow industry to proceed on its own.

Representative Van Zandt. What part will Government play when industry takes over this project?

Colonel Cook. Then, sir, we will be interested in our normal role. The Army, as a large food consumer, is interested in logistical applications of handling and packaging and moving food.

Representative Price. Colonel, if you are so certain of that schedule, why do you not just put a little more effort in this thing and develop it in the next year or so and have it fully developed, instead of such a leisurely schedule?

Colonel Cook. It is not a leisurely schedule, sir. There are things in the program which require time. One is the design and construction of the pilot plant facility. We feel the earliest possible time this could be completed and placed into operation is October 1958. This is the hinge point of the program.

As soon as that pilot plant is available we will have sufficient capacity to process sufficient foods to supply all of our research contracts and also to test the food in our logistic system.

Representative Price. You will not be using it after you have phased out of the program. Who will be using that pilot plant?

Colonel Cook. We will not be phased out of the program in 1959.

Representative Price. Maybe there is some misunderstanding. Are you phasing out of the program? Are you working toward that end, or are you intending to go into this with both feet and try to develop it as quickly as possible?

Colonel Cook. We are trying to develop as quickly as possible the capacity within industry to furnish the Army with radiation preserved foods.

Representative Price. Of course that is the plan. We are talking now about the research phases. Are you in any way gearing your activities to phase out the research end of this program within a period of time?

Colonel Cook. Our plan contemplates phasing out our interest in the program, that industry and other Government agencies will assume their responsibilities.

Representative Price. That is all well and good. But I understand this program, if it is of great importance, is of greatest importance to the military, for obvious reasons. The military will probably be the one who most need something like this. In time of war it would be of inestimable value to them.

To me, then, it would seem that you would not want to turn this program over to anybody else. You would want cooperation and assistance from them, but industry would not have the same urgency to develop this program as you would because they think of the commercial side. They have frozen foods now. They are not anxious to kick them off the shelf right now. So they do things in a different fashion. But yours is one of urgency. Yours is one to meet a challenge if it does come to meeting it.

Now, is attention and thought being given to something like that?

Colonel Cook. That is correct, sir. You will find the Army is supremely cognizant of the fact that the potentials of this program in a new environment, a mobile environment, are very large. If we can get to the point of moving troops very rapidly in a mobile situation independent of refrigerated storage and handling and shipping, this would be a tremendous advantage in the logistic system.

Representative Price. If I were the Army, I certainly would not want to let go of this research program until it is a proven thing, and then let industry have it to produce your foods when you need them. But, by gosh, I would be certain I had this program wrapped up.

Representative Van Zandt. Do you expect to have it wrapped up in 1959 or 1960?

Colonel Cook. We are confident of that with the progress we have made to date.

Representative COLE. I wish I could share your enthusiasm and your optimism.

Representative PRICE. Is that an agreed thing? Do you agree with that, Dr. Siu, that this thing will be proven within the next 4 years, 1960?

Dr. SIU. I think the technology will be at such a state that industry should be willing to take over.

Representative COLE. He said it would be.

Representative PRICE. Do you think it is a calculated risk the military can take?

Dr. SIU. If in the next year or so it turns out that our optimism is not justified, we will request that the plan be changed, that we extend our time of dominance. I think the point that Colonel Cook was trying to make is that the military should gradually phase out of a position of dominance. I think the "position of dominance" is the key phrase, and the question at hand is the proper time to drop that position of dominance.

Representative PRICE. Do you not think the proper time to drop that position of dominance would be when you have this program so well proven you knew it would be available when you needed it?

Dr. SIU. If it is a guaranteed proposition before we drop it, then it may be some years, sir.

Representative PRICE. Is that a normal practice, General Hastings, within the Quartermaster Corps research program, to take these things up to a point and then turn them over to private industry? I am talking not only of this program but all research programs.

General HASTINGS. I think, sir, it depends very much on the scope and size of the program. I think that is where we have created a misunderstanding before the committee, sir. We have indicated to you, unfortunately, that we are trying to get out of this thing, and we are not. We are trying to lead the parade in every which way.

Representative PRICE. We are not objecting to private industry getting into this picture. We are not objecting at all. We would like to see it come in. As a matter of fact, we encourage them to come in.

General HASTINGS. That is correct; and that is what we are trying to do, too. We are trying to increase the enthusiasm outside the military for the program, but we are planning to go ahead and push just as vigorously as we possibly can.

We have a very vital interest in the whole thing, and we intend to go right after it.

It is very much like the whole refrigeration program in the United States today. We are still vitally interested in developing and improving refrigerating means.

Representative PRICE. You are still working on refrigeration?

General HASTINGS. Yes, sir; we are studying all the time on it, sir.

Representative PRICE. You do not want to phase out of this program then, do you?

General HASTINGS. No, sir; we do not want to. We want to increase our activity in it; but we believe it may be just as big as the whole refrigeration industry in the United States, so some of it goes beyond our scope.

Our interests are still just as vital and we are going to push just as hard as we can.

Representative COLE. What is an illustration, if you can give us one, of the interest by commercial enterprises in this program of food sterilization by radiation?

Colonel COOK. There is an exhibit included in the brochure which has a list of all the collaborate arangements we have with industrial concerns, and it compares the number we had in 1955 with the number we had in 1956. In this group of collaborative arrangements, the number we have gives us the degree of confidence that we are expressing. It is this movement of industry in seeking information and wanting to collaborate with us which gives us the basis of our confidence.

This list, incidentally, will grow through the years, and the amount of participation dollarwise will increase; and, let's say, the diversification of interest and products throughout our food line will increase.

Representative COLE. That is your chart?

Colonel JACKSON. That is the chart in my statement. There is one additional thing. The military have a very vital interest in this program; I do not think we have reached the point where we can walk completely out of the program. As I gather, that was your fear.

We feel this is a very large program which encompasses both military and civilian applications. We intend to solve the military applications, and we intend to stay in it to solve the military applications. We do not at this time have the funds, nor does the Defense Department feel that they should divert the funds from military problems to solve the civilian problems in this field. We are looking at this project as a very large scope, having wide ramifications throughout the civilian economy as well as the military.

We will solve the military problems. That is why we are encouraging industry to come in and solve the civilian problems, and also the other agencies of the Government which have civilian interests more than military interests.

But there is no idea of us getting out of this program at all. We want to solve the military problems.

Representative VAN ZANDT. Is it not true that 1960 is your date?

Colonel JACKSON. That is right.

Representative VAN ZANDT. On some of these food items by 1960 you expect to have a perfected method of sterilizing them?

Colonel JACKSON. That is right.

Representative VAN ZANDT. For example, let us consider the potato.

Colonel JACKSON. Yes, sir.

Representative VAN ZANDT. Instead of ordering dry potatoes to be sent to the troops, it will be possible in tropical areas, and so forth, to simply say to industry, "The method has been perfected now to sterilize the potatoes; you sterilize and ship to us so many thousands of tons of potatoes"?

Colonel JACKSON. That is correct.

Representative VAN ZANDT. Instead of ordering "dry" potatoes, you will order the "sterilized" potatoes?

Colonel JACKSON. That is right. We will make specifications and buy them.

We, as a consumer, have a tremendous influence on leading industry into this. But there are so many technical problems. That is the reason we are solving those first so we then can have a specification that is capable of being carried out by industry, and then we can buy the product we want to solve a military problem.

Colonel Cook. I would like to summarize our future plans by exhibit 250. This exhibit gives the objectives of the program over a period of 5 years, 1956–60.

In 1956, in the survey on 80 foods we will continue wholesomeness tests and human feeding tests, and intensify the campaign to inform the American businessman, and complete the preliminary plans for the Army Ionizing Radiation Center.

In 1957 the construction will begin on the Army Ionizing Radiation Center, a Joint Atomic Energy Commission-Department of Defense project. Research emphasis will be placed on 20 selected foods, and foreign trade fairs will include this process in its exhibits.

In 1958, we must develop packaging requirements, conduct storage and handling studies, perform limited troop taste testing on irridiated foods and place the Radiation Center into operation.

In 1959, pilot-plant research on 20 foods and pilot-plant production on 10 foods must be conducted to collect economic-cost data and engineering-design data for commercial plants.

Representative Cole. What do you mean by pilot-plant production?

Colonel Cook. The design of this plant is intended for a peak capacity of 1,000 tons per month. This does not mean it would run continuously at 1,000 tons per month, but the design characteristics are such that if run for a reasonable period of time it would be equivalent to a thounsand tons per month.

Representative Van Zandt. What is the production capacity at this date?

Colonel Cook. Approximately 30 tons per month. This is really research volume.

Representatice Cole. What is your production capacity?

Colonel Cook. Approximately 30 tons per month.

Representative Cole. And this plant will be what?

Colonel Cook. A thousand tons per month.

Representative Cole. Is that a Government plant or private plant?

Colonel Cook. This will be a Government-owned, contract-operated facility.

Representative Cole. The production plant?

Colonel Cook. The thousand-ton-per-month plant.

Representative Cole. Will that be located in the proximity of the research plant?

Colonel Cook. This is the plant, sir, you were discussing with Colonel Jackson.

Representative Cole. Is that a production plant?

Colonel Cook. This is not a production plant; this is a pilot plant, a pilot plant which will satisfy our research requirements and satisfy economic cost data and engineering design data requirements, and process sufficient foods for all of our research contracts, and also enough foods to put in the logistic pipeline to see whether it actually stands up under handling and storage conditions, and also feed to limited troops for testing.

During this year, and that is 1959, industry must assume a larger role.

In 1960, user acceptance clearance should be obtained on some foods. Troop consumption experiments will be conducted. Economic analysis for 10 foods, based on pilot plant production experience, will be

completed. Production of irradiated foods by industry should begin. Procurement by the Army of a few selected foods should begin during 1960.

No greater expression of our optimism than such a statement of definite practical target objectives can be made.

It has been the Army's considered opinion that a broadened program in radiation preservation of food in industry and Government will provide for a much faster rate of progress, represent a significant contribution to our atoms-for-peace program and efforts, and utilize more effectively the combined technological talents of other agencies, and finally insure the rapid acceptance and transition of the process into industry.

The Army is deeply appreciative to the subcommittee for its interest in this program and certainly has valued your wise counsel.

Mr. Chairman, thank you for the opportunity to present the program.

I would like to introduce one final person who has been here, Dr. Stanhope Bayne-Jones, who is scientific advisor to the Surgeon General of the Army and has contributed considerably to the wholesomeness tests, and counsel in that particular area for the program.

We are open for any questions you may have.

Representative PRICE. Do you work closely also with the Bureau of Public Health?

Colonel COOK. Yes, sir. We have definite contacts with the United States Public Health Service through the Department of Health, Education, and Welfare, and the Food and Drug Administration. James Terril in the Radiological Health Division of that Department or that agency is a personal friend of mine, and we have direct contact with him and his activities.

Representative PRICE. Do they give consideration even at this early stage of arriving at various standards in irradiated foods?

Colonel COOK. The Surgeon General of the Army works very closely with the Food and Drug Administration in developing the protocol for the testing of and experimental procedures for the human feeding and the wholesomeness tests, which must be completed so the Food and Drug Administration will actually clear the foods when we have completed our studies.

Representative PRICE. But you work with them from day to day in the program so that you always coordinate in your activities?

Colonel COOK. Yes, sir. They have membership actually on a task group which is composed of quartermaster people, Surgeon General people, and Food and Drug Administration people, and they meet frequently, discuss these matters, and arrive at the standards of test procedures which will meet not only our own requirement within the Army but meet also the requirements of the Food and Drug Administration.

Representative PRICE. Are there any further questions?

Representative VAN ZANDT. Colonel, are you getting sufficient funds to operate the program?

Colonel COOK. I would say, sir, that we are not. If we should consider the question from the overall program standpoint, we are not adequately funded.

This is a conditioned answer and I would like to explain it. We have encountered some difficulty in getting all the funds we needed. But let me review some of the things that have occurred under the stimulus of this subcommittee last May.

We recognized at that time we had to review the program from an overall standpoint beyond the Army interests, and we took certain definite action to provide for this.

We suggested the formation of a national committee to guide the program, develop broad policy.

We also suggested a broader funding base, including funding by other Government agencies and industry. And we suggested the phasing of the program at that time from the Government environment into the industrial environment without sacrificing the rate of progress.

I would like to review what has happened since then because it definitely indicates the interest of other Government agencies and their desire to participate.

In November, we briefed the Atomic Energy Commission on this program, and they acted very swiftly. The following day they submitted to the Bureau of the Budget an item for the reactor portion of the pilot-plant facility, a $3 million cost, which is budgeted in 1957.

During the months of January and February, we briefed the Departments of State; Health, Education, and Welfare; Commerce; Agriculture; and our own Army Scientific Advisory Committee. Each of these agencies indicated their intense interest in participating in the program.

We formed, instead of a national advisory committee, an Interdepartmental Committee on Radiation Preservation of Food, which has membership from all of these Government agencies at the Assistant Secretary level.

This Interdepartmental Committee will be concerned with developing policy in guiding the program through these 5 years. It is this committee that Dr. Siu is executive secretary pro tempore. This Committee is chairmaned at the present time by Mr. William Martin, Director of Research and Development of the Department of the Army.

Within the Army we also briefed the Deputy Chief of Staff for Logistics on the logistic implications of this program, and as a result of that briefing we are able to reprogram in 1956 $500,000, which includes $200,000 for the design costs of the facility and $300,000 for the purchase of a linear accelerator.

We have also reprogramed in 1957 $2 million for the nonreactor portion of the facility; in 1958, $2,060,000 for the nonreactor portion of the facility; and subsequent years the cost for maintenance and operation of the facility.

So you will notice we have in the program sufficient funds, we feel, to build and operate this facility and place it into operation by approximately October 1958.

However, we have justified and submitted a request for additional financing in 1956, as we reported to you on February 1, of $1,125,000. Of this amount the $500,000 which has been reprogramed within the Army has cut the requirement, let's say, $600,000.

The reduced amount, $600,000, was justified to the Assistant Secretary of Defense, Research, and Development, who approved the release of these emergency funds to the Army to the Bureau of the Budget.

This approval was turned down by the Bureau of the Budget. We are now in discussions with the Bureau to release these funds. We feel that the reason the Bureau of the Budget turned us down is because they did not fully understand the significance of getting the funds on an emergency basis for this program in 1956. We feel that they will approve the additional amount.

Representative COLE. What makes you be so optimistic that they have changed their minds? Have they told you so?

Colonel COOK. There have been discussions between their personnel and the Assistant Secretary of Defense, comptroller personnel regarding this item, and they have come to a mutual understanding on this amount of money. It was justified on the 3d of February of this year. The funds, I must say, are not yet available to the Department of the Army. They do represent funds which would cover certain important tasks that must be completed in advance of the availability of facility.

We feel that these funds are necessary and are needed. But, as you review the total funds that have been made available and the funds which we secured for 1957 and are going to program in 1958, we are substantially funded. However, we have a strong opinion that this $600,000 in 1956 which would provided for a mild acceleration of the program is necessary.

I might say at this point that we are attempting through the Interdepartmental Committee on Radiation Preservation of Food to increase the participation of other Government agencies. This Committee has just recently been formed, and we should not judge in advance the ability of this Committee to actually get a stronger participation by Government agencies. We feel that there will be a noticeable increase in participation to the benefit of the program, and we feel to the benefit of a program of a peaceful development nature.

Representative VAN ZANDT. With respect to the $600,000 you mentioned, if you are unable to get the authority to spend it, what effect is it going to have on your reactor program which is scheduled here for 1958?

Colonel COOK. These funds, sir, will provide for certain elements that must be satisfied. First, we must have a dosimeter.

Representative VAN ZANDT. Will you explain its purpose?

Colonel COOK. A standard dosimeter which can measure radiation in million rep range, sufficiently accurate to control our dosage. This is one item.

The other: We should start at the present time sufficient wholesomeness research on certain food commodities so we will have Food and Drug Administration clearance and Surgeon General clearance by the time we process this food in the plant. This is a necessary item.

We have also found there is a strong relationship between the storage at normal room temperatures and the flavor-odor problem. We would like to investigate that with a large amount of interest and a larger number of contracts.

Finally, we did mention that we must solve our packaging problem, and in the packaging problem area we find there are many types of packaging containers, flexible packaging materials which would en-

hance the process. We would like to investigate that more fully and thoroughly.

So overall these, let us say, one-time requirements would amount to about $600,000 over and above our current scheduled program.

Representative VAN ZANDT. Is it not true in the sterilization of meat that the type of material used in the packaging of it is a very important problem?

Colonel COOK. Yes, sir; because consumer acceptance is going to be based on whether the meat appears to be good. I would say that the housewife would want to see a piece of steak through a transparent flexible container before she buys it. It is not inconceivable, however, that meat would be processed in a can and marketed as canned meat. Then the dependence of the housewife on the product would be on the reputation of the concern in putting out a significantly uniform and good product all the time.

Representative VAN ZANDT. Would you agree with me, Colonel, if I were to say that the failure of the Bureau of the Budget to make available the $600,000 is definitely interfering with the progress of this sterilization program?

Colonel COOK. I would say that it does interfere with the rapid rate of progress of the program. I would temper that to say it is not a critical interference. It interferes with rate or progress.

Representative PRICE. Thank you very much, Colonel Cook.

General HASTINGS. Congressman Price, I would like to present to the subcommittee this brochure entitled "Effect of Radiation Sterilization and Preservation on the Wholesomeness of Foods." That concludes our presentation, sir.

Representative PRICE. Thank you very much, General, for a very interesting presentation. We will insert the brochure in the record at this point. I regret the fact it was not possible for me to be here during the early stages of it, but I assure you I will read these brochures which you have presented. It was necessary for me to attend the Armed Services Committee on a matter of importance.

Thank you, General Hastings, Colonel Jackson, and all of you gentlemen for a very fine presentation.

(The material referred to follows:)

EFFECT OF RADIATION STERILIZATION AND PRESERVATION ON THE WHOLESOMENESS OF FOODS

(Prepared by Research and Development Division Office of the Surgeon General, Department of the Army, Washington 25, D. C.)

The primary objective of the Surgeon General's program is to determine whether or not irradiated foods may be fed safely to humans. During the past year this program has been continued at 13 universities and privately sponsored research institutes and at the Medical Nutrition Laboratory, Fitzsimons Army Hospital (exhibit 251). In the design of certain experimental phases of the program, the Food and Drug Administration of the Department of Health, Education, and Welfare and the University of Chicago Statistical Research Group have aided materially by their advice and suggestions. The Meat Inspection Division

of the United States Department of Agriculture has been apprised of the progress in the program.

This broad program, designed to prove the safety characteristics of irradiated and preserved foods, has been directed through two major lines of approach: (*a*) potential toxicity, and (*b*) nutritional adequacy of radiation sterilized and preserved foods.

The research program concerned with potential toxicity of irradiated foods may be further subdivided into three distinct phases: (*a*) toxicity as determined by short-term feeding experiments with experimental animals and human test subjects, and (*b*) obscure toxicity as detected by long-term feeding experiments, and (*c*) carcinogenicity as determined by tests on certain animal species.

EXHIBIT 251

List of participating research institutions, Surgeon General's program, irradiated foods

Institutions	*Areas of research*
1. Columbia University	Vitamin E studies.
2. Alabama Polytechnic Institute	Micronutrients.
3. University of Illinois	Macronutrients.
4. Texas A. and M. College	Longevity, reproduction, lactation.
5. University of Michigan	Long-term feeding, rats and chickens.
6. Oregon State College	Long-term feeding, pork and organ meats.
7. University of California at Los Angeles.	Feeding studies, irradiated fats.
8. Wisconsin Alumni Research Foundation.	Carcinogenicity.
9. Armour Research Foundation	Short-term feeding (rats).
10. Cornell University	Long-term feeding, dogs.
11. University of Rochester	Digestibility studies, dogs.
12. John Hopkins University (McCollum Pratt Institute).	Feeding studies on degradation, products of irradiation.
13. University of Colorado, Medical Nutrition Laboratory.	Long-term feeding (rats), short-term feeding (humans).

INDUCED TOXICITY

The short-term feeding experiments on irradiated foods initiated early in 1954 were designed for securing toxicity clearance on a wide spectrum of irradiated foods to permit testing by a palatability panel at the Quartermaster Food and Container Institute for the Armed Forces in Chicago, as well as to permit the testing of these foods on human volunteers at the metabolic ward, Medical Nutrition Laboratory, Fitzsimmons Army Hospital in Denver, Colo. Through these short-term experiments, 44 foods have been tested and forty irradiated foods have been cleared. The remaining four foods, turkey, spinach, cranberries, and jello powder, are being currently retested. On the basis of similarity in composition and type, an additional 59 irradiated foods have been cleared by extrapolation for palatability panel evalution.

Long-term feeding experiments on irradiated organ meats, butterfat, pork, and beef now in progress at several universities have indicated that these foods are satisfactory when fed at high levels in the diet to successive generations of rats. In another investigation in which rats were fed a nutritionally adequate diet composed entirely of irradiated foods (treated at 6 megarep dosage) no adverse effects developed from feeding irradiated foods to the first two generations (exhibits 252 and 253). Similar studies designed to test longevity, reproduction, and lactational performance using an irradiated synthetic animal ration have likewise demonstrated no ill effects after feeding this ration through three generations. These latter experiments have been conducted on rats, mice, and chickens.

EXHIBIT 252

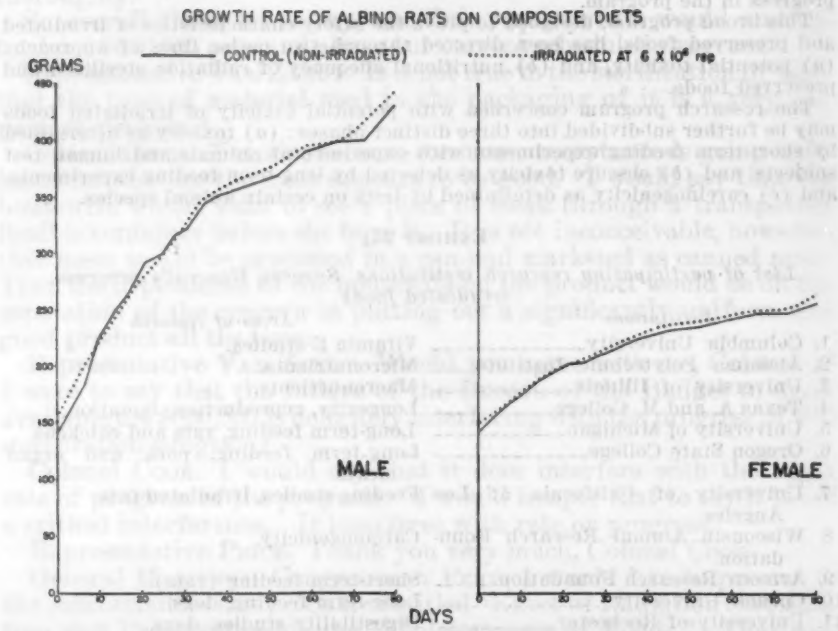
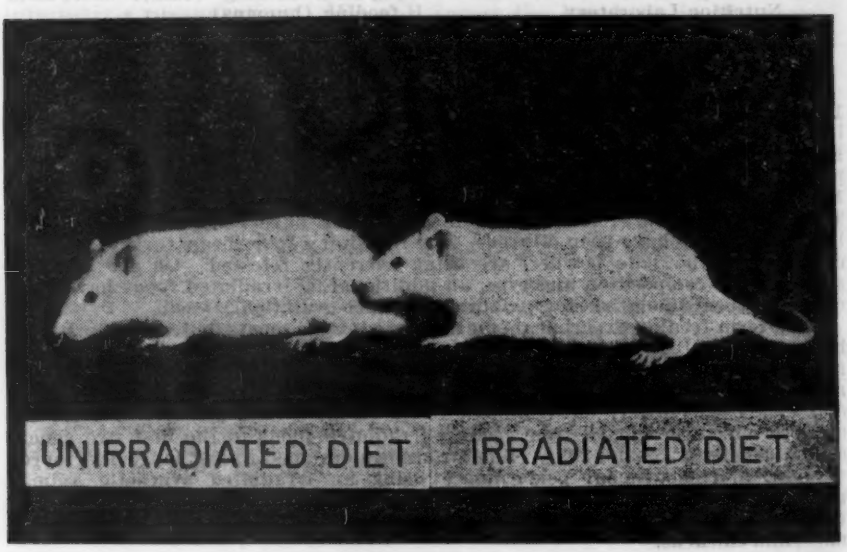


EXHIBIT 253.—Comparison in growth of rates on unirradiated and irradiated diets.



A diet in which 50 percent of the calories are supplied by irradiated ground beef has been fed to female beagle pups for 9 months without any observed differences in growth rate or feed consumption from feedng irradiated and non-irradiated ground beef. The irradiated beef was treated at dosages of 3 and 6 megarep.

The data thus far obtained from animal-feeding experiments do not indicate any significant production of toxic compounds by radiation sterilization or preservation. The subtle nature of the changes brought about by irradiation, however, requires the extension of these studies for longer feeding periods, in order to insure that foods sterilized or preserved by ionizing radiations may be safely consumed by human populations. This second phase of long-term feeding studies, now the most important area of work, has been initiated. A long-term rat-feeding study employing potatoes treated with the radiation dosage necessary for sprout inhibition (20,000 to 40,000 rep) has been underway at the University of Michigan since December 1955. Another rat-feeding study utilizing ground-pork radiation sterilized with 3 to 6 megarep and subsequently stored at 70° C. was initiated at the Oregon State College in January 1956. Contracts have been negotiated for conducting similar long-term feeding studies on rats and dogs with irradiated beef, flour, chicken, and green beans stored for a minimum of 3 months at 70° F.

One of the most important questions to resolve in the testing of a newly processed food is that of carcinogenicity or the possibility of spontaneous tumor formation. Mice were painted and injected with extracts of egg, yeast, and pork sterol and rats were fed these products at high levels. While the radiation dosage (10×10^6 rep) was considerably higher than that contemplated for commercial processing of foods (3×10^6 rep), preliminary results indicate no carcinogens formed or any tumor formation in the animals fed the treated diets.

NUTRITIONAL ADEQUACY

The nutritional properties of fats, protein, and carbohydrates that have been irradiated have been studied, and it has been observed that the energy value of several meat, vegetable, and dairy products has remained unaltered by irradiation. The biological value of protein, a measure of the utilization of the protein, has also been found to be similar for nonirradiated and irradiated beef, lima bean, and pea proteins. The biological value of irradiated milk protein is slightly less than that of canned milk.

Although the macronutrients have been shown to remain essentially the same following irradiation, some small losses in micronutrients and vitamins have been reported. Irradiation processing of foods apparently effects some destruction of fat-soluble vitamins (vitamins E and A). The destruction of the water-soluble vitamins is, in general, not as great by radiation sterilization as by heat treatment (exhibit 254). Thiamine suffers the greatest destruction from radiation sterilization, of the order of 65 percent at 3 megarep, a value comparable to the destruction resulting from current commercial preserving techniques. The pyridoxine content in radiation sterilized beef has been shown to be reduced by 25 percent, whereas the reduction of pyridoxine in heat-treated beef is reported to be 30 percent. Niacin is relatively resistant to radiation sterilization in contrast to heat treatment. The other water-soluble vitamins, such as riboflavin and folic acid, which have been studied, do not exhibit appreciable destruction, whereas losses due to heat sterilization occasionally amount to 35 percent.

EXHIBIT 254

Comparative data on vitamin destruction in foods

Vitamin	Heat treatment	Radiation sterilization
	Percent	*Percent*
1. Thiamine	65	63
2. Riboflavin	20	8
3. Pyridoxine	30	25
4. Niacin	30	0-3
5. Folic acid	35	0
6. Vitamin E		[1] 10-30
7. Vitamin A	20	[1] 8-29

[1] 80,000 r/hour on dairy products.

HUMAN FEEDING OF IRRADIATED FOODS

Once the more promising irradiated foods have successfully passed the 8 weeks animal-feeding experiments and the QMF and CI palatability panel evaluations, they are fed on the metabolic ward, at the Medical Nutrition Laboratory, Fitzsimons Army Hospital, Denver, Colo., to human volunteers, all members of the Mennonite Church. Special credit must be given to Bishop E. M. Yost, of the Mennonite Church in Denver, Colo., and to Mr. H. O. Lail, of the State selective service, as well as to Maj. Gen. Lewis B. Hershey, Director of Selective Service, Washington, D. C., for their help in enlistment of these volunteers (exhibit 255). These human volunteers have been unusually cooperative and enthusiastic, qualities without which these studies would never have been possible.

EXHIBIT 255

HUMAN VOLUNTEERS ON IRRADIATED FOODS STUDY

First irradiated food study May 9 to June 14, 1955

1. John Meyer, Sterling, Ohio
2. Virgil Erb, Geneva, Nebr.
3. Eldon Miller, Albany, Oreg.
4. Arlie Thiessen, Conway, Kans.
5. Harley Redigar, Miller, S. Dak.
6. Kenneth Goertzen, Hampton, Nebr.
7. Harry Pankratz, Inola, Okla.
8. Abie Siemens, Buhler, Kans.
9. George Smith, Meno, Okla.

Second irradiated food study, September 12 to October 17, 1955

1. John Meyer, Sterling, Ohio
2. Virgil Erb, Geneva, Nebr.
3. Harley Redigar, Miller, S. Dak.
4. James Prehiem, Moundridge, Kans.
5. Abie Siemens, Buhler, Kans.
6. Harry Leppke, Corn, Okla.
7. Richard Holzrichter, Buhler, Kans.
8. Marlin Maurer, Louisville, Ohio
9. Wilbert Schmidt, Ulysses, Kans.
10. Robert Unruh, Tampa, Kans.

Third irradiated food study, January 26 to February 27, 1956

1. John Meyer, Sterling, Ohio
2. Virgil Erb, Geneva, Nebr.
3. Harley Redigar, Miller, S. Dak.
4. James Prehiem, Moundridge, Kans.
5. Abie Siemens, Buhler, Kans.
6. Harry Leppke, Corn, Okla.
7. Richard Holzrichter, Buhler, Kans.
8. Marlin Maurer, Louisville, Ohio
9. Robert Unruh, Tampa, Kans.
10. Gene Heinrichs, Wolf Point, Mont.

Fourth irriadiated food study

1. Virgil Erb, Geneva, Nebr.
2. Harley Redigar, Miller, S. Dak.
3. James Prehiem, Moundridge, Kans.
4. Harry Leppke, Corn, Okla.
5. Richard Holzrichter, Buhler, Kans.
6. Marlin Maurer, Louisville, Ohio
7. Robert Unruh, Tampa, Kans.
8. Gene Heinrichs, Wolf Point, Mont.
9. Jerry Plett, Lehigh, Kans.

A. Method of studies

Each study encompassed a period of approximately 36 days. During the first 15 days, half the subjects were fed irradiated foods, and the other half received identical nonirradiated foods. Following a rest period of approximately 6 days, the two groups were reversed so that those on irradiated foods

shifted to the control and vice versa. At no time were the subjects informed as to which diet was irradiated. A battery of tests (exhibit 256) was used throughout the study to provide for the safety of the subjects and to obtain information regarding the possible toxic effects. Photographs depicting some of these procedures are enclosed as exhibits 259 through 266. These tests include frequent physical examinations, blood counts, studies of liver and kidney function, electrocardiograms, basal metabolic rates, and X-ray studies. In addition, extensive energy balance studies of the diets were made as well as analyses of the excreta. By this means, accurate information concerning the food energy available to the body for its use was obtained for both irradiated and control foods.

EXHIBIT 256

Medical procedures followed for human test subjects

1. General physical examination	Weekly during studies.
2. Chest X-ray	Before each study.
3. Liver function test	Weekly during studies.
4. Kidney function test	End of each period.
5. Blood counts	Twice weekly.
6. Electrocardiograms	End of each period.
7. Urinalysis	Do
8. Dental examinations	Before and after each study.
9. Eye examinations	Do
10. Body weight	Daily during studies.
11. Blood pressure	Twice daily during studies.
12. Temperature, pulse, respiration	Do

NOTE.—After men are discharged from the project they are requested to return to Fitzsimons Army Hospital for follow-up examinations at 3-, 6-, and 12-month intervals.

The first study, May 9, through June 14, 1955.—Eleven food items were irradiated at 3 million rep and fed as 35 percent of the total calories of the diet. These food items are outlined in exhibit 257. Physical examinations and laboratory tests revealed no significant changes which could be ascribed to the irradiated foods. The metabolizable energy of the irradiated diet was not substantially different from that of the control nonirradiated diet.

EXHIBIT 257

Feeding studies, irradiated foods, human volunteers

First irradiated food study, May 9 to June 14, 1955

Bacon	Peaches	Cereal bar
Beef, ground	Strawberries	Bread
Haddock	Green beans	Powdered milk
Ham, ground	Beets	

11 foods. (*Irradiated foods furnished as 35 percent of calories of diet.*)

Second irradiated food study, September 12 to October 17, 1955

Same items as above plus:

Sausage	Pound cake	Shrimp
Macaroni	Green peas	Dried pears

17 foods. (*Irradiated foods furnished as 65 percent of calories of diet.*)

Third irradiated food study, January 26 to February 27, 1956

Corned beef	Celery	Crackers
Carrots	Brussels sprouts	Tuna
Mushrooms	Melon balls	Frankfurters
Potatoes, white	Cherries	Dessert powder
Cauliflower	Salmon	Rice
Cabbage	Lima beans	
Asparagus	Peanut butter	

Foods from previous study:

Ground beef	Peaches	Pound cake
Pork sausage	Powdered whole milk	Macaroni
Bacon	Pears	Bread

28 foods. (*Irradiated foods furnished as 80 percent of calories of diet.*)
Total number of different foods tested in all studies to date, 36.

Fourth irradiated food study, to start about April 2, 1956

Additional items:

Sweetpotatoes	Corn	Strawberry jam
Peas	Dried apricots	Sugar
Nut roll	Tenderloin steaks	Ham steaks

To total 40 items. (*Irradiated foods to furnish 100 percent of calories of diet, except condiments.*)

In the second study, September 12 to October 17, 1955, the percentage of calories furnished by irradiated food, some 17 items, was increased to 65 percent of the total calories. The plan of the study was identical to that of the first. Again, physical examinations and tests revealed no significant changes attributable to irradiated foods. Likewise, the metabolizable energy of the irradiated diet was similar to the control diet.

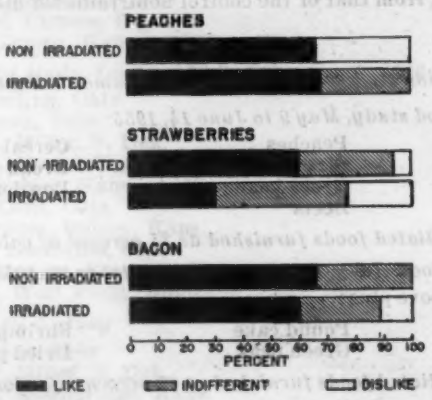
The third study, January 26 through February 27, 1956, included 28 irradiated food items constituting approximately 82 percent of the total calories offered. The physical examinations and chemical analyses again indicate no ascribable toxicity to irradiated foods.

The fourth study, April 4 through May 8, 1956, employed 40 irradiated food items comprising 100 percent of the total calories. Evaluation of the data has not yet been completed.

B. Acceptability

Of these food items which thus far have been subjected to statistical evaluation, most of the control and irradiated foods were equally acceptable to the volunteer subjects. In the case of irradiated strawberries, however, the first study demonstrated a statistical preference for the control item over the irradiated item. This preference is illustrated in exhibit 258. Similarly irradiated powdered milk when flavored with cocoa rated somewhat lower than the control powdered whole milk issued.

EXHIBIT 258. Acceptability of typical irradiated and nonirradiated foods: percentage distribution of ratings by test subjects.



C. Metabolizable energy

No differences could be discerned between the available energy of nonirradiated or irradiated foods. However, for a few of the food items there were small but statistically significant differences in the caloric value per gram of wet food between irradiated and control items; namely, strawberries, powdered milk, green beans, ground beef, ground ham, and haddock. The exact significance of these small differences is not clear.

D. Report on 3- and 6-month reevaluation of test subjects

Five of the first group of human volunteer subjects have been examined at 3- and 6-month intervals since the termination of their service at the metabolic ward, Medical Nutrition Laboratory. No evidence of residual toxic effects from the consumption of irradiated foods has been observed.

E. Medical supervision

In addition to expertly trained dietitians, nurses with special training in nutrition and metabolism, and a trained physician in constant attendance on the metabolic ward, the Medical Nutrition Laboratory has the benefit of consultation with the faculty of the University of Colorado Medical School.

F. Projected plans

We plan to extend the investigations on sterilized and preserved irradiated foods stored under field or combat conditions (3 to 6 months at room temperatures) through a continuation of the feeding studies on laboratory animals and ultimately human volunteer subjects for longer periods.

EXHIBIT 259. Feeding of test meal containing irradiated foods to human subjects.

EXHIBIT 260. Feeding of test meal containing irradiated foods to human subjects.

EXHIBIT 261. Preparation of diets for test subjects.

EXHIBIT 262. Collection of expired oxygen from test subjects for basal metabolism tests.

EXHIBIT 263. Electrocardiogram on test subject by medical officer in charge of metabolic ward.

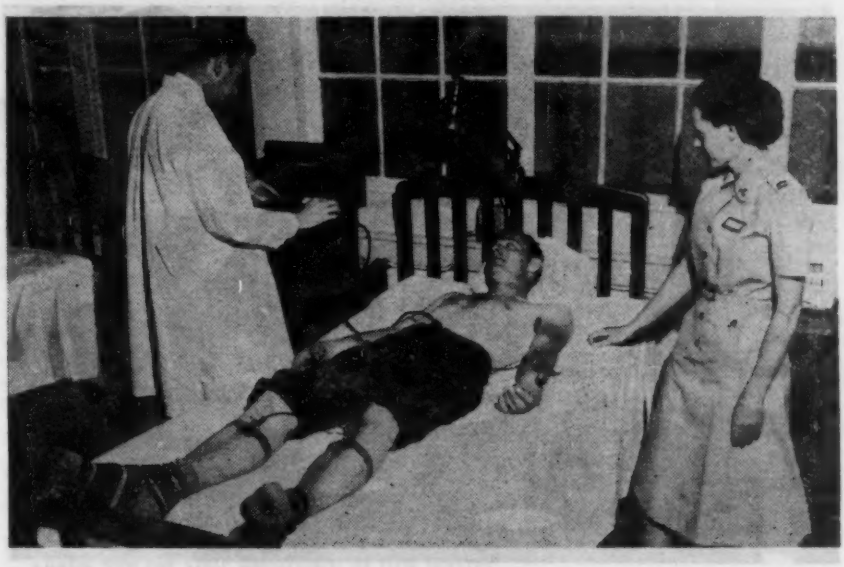


EXHIBIT 264. Injection of dye for kidney function test on human test subject.

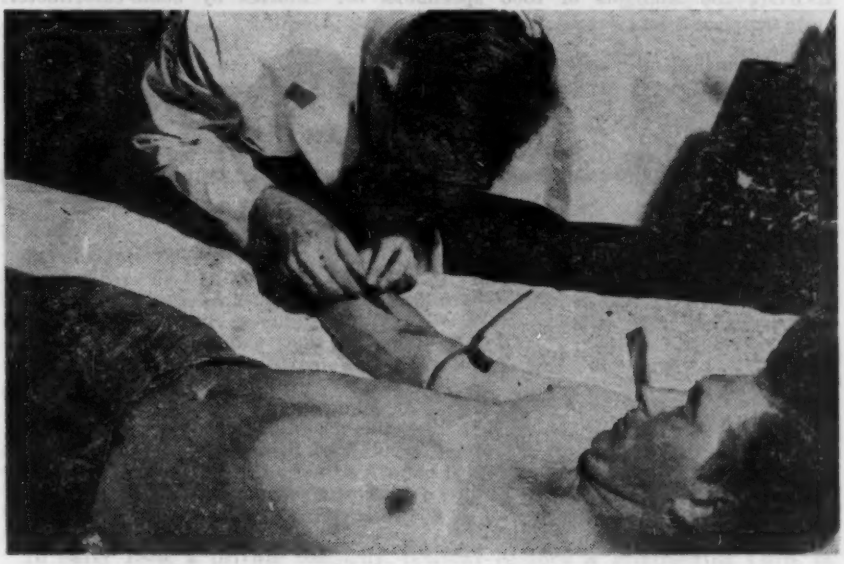
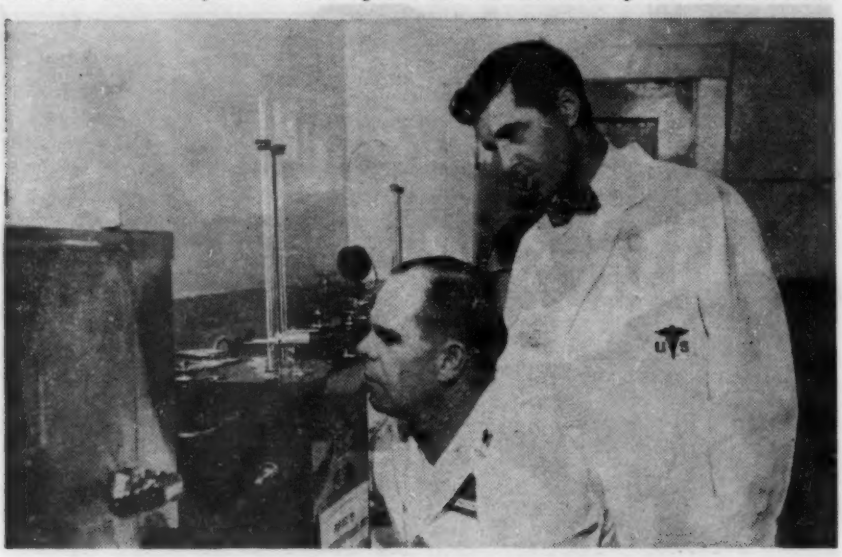


EXHIBIT 265. Laboratory technician prepares urine specimen for subsequent analysis.

EXHIBIT 266. Analysis of food specimens for calories by bomb-calorimeter.



(Whereupon, at 11:58 a. m., Friday, June 8, 1956, the subcommittee adjourned to reconvene at the call of the Chair.)

APPENDIX

JUNE 26, 1956.

Hon. LEWIS L. STRAUSS,
Chairman, United States Atomic Energy Commission,
Washington, D. C.

DEAR MR. STRAUSS: During the recent hearings held by the Research and Development Subcommittee to receive progress reports on medical and biological research work being done with radioactive isotopes, the scarcity of two isotopes was mentioned.

The members of the subcommittee are concerned over both the scarcity and high cost of the stable isotope arsenic 74. We were informed that the AEC does not now produce any of this isotope, and the commercial facilities to produce it are extremely limited with a resultant high cost.

We are likewise concerned over the apparent limitations imposed upon the widespread use of cobalt 60 for teletherapy caused by the limited irradiation facilities, particularly those for the production of high activity sources.

It would be appreciated by the subcommittee if you could give us your suggestions on how these limitations can be overcome.

Thank you for your assistance in this matter.

Sincerely yours,

MELVIN PRICE,
Chairman, Subcommittee on Research and Development.

UNITED STATES ATOMIC ENERGY COMMISSION,
Washington 25, D. C., July 11, 1956.

Hon. MELVIN PRICE,
House of Representatives.

DEAR MR. PRICE: The information given below is submitted in response to your letter of June 26, 1956, regarding the supply of the radioisotopes arsenic 74 and cobalt 60.

Arsenic 74

The Atomic Energy Commission initially undertook the production and processing of arsenic 74 together with other cyclotron isotopes in 1949, the purpose being to assist research by providing radioisotopes which could not be produced in a nuclear reactor or could not be prepared to meet activity specifications. Moreover, these isotopes were not then obtainable from commercial sources. Under this program the Atomic Energy Commission prepared, irradiated, and processed the material.

When the Atomic Energy Commission first undertook to supply arsenic 74 the price was $75 per megacycle which was substantially less than cost. The $75 price remained in effect until July 1954 when it was increased to $200 per megacycle to bring it more in line with Atomic Energy Commission's costs; however, later studies disclosed that even this price was below cost. Shipments by Atomic Energy Commission during the years 1950 to 1955, inclusive, totaled 6.31 megacycles.

In early 1955, a private company, Nuclear Science & Engineering Corp. of Pittsburgh, informed the Atomic Energy Commission of its intention to supply arsenic 74 as a processed radioisotope at a price of $200 per megacycle. In view of the Commission's policy to avoid competing with private suppliers of materials, it was decided to discontinue the processing and sale of cyclotron-produced isotopes. The new policy became effective 90 days after the Commission's decision had been publicly announced.

Even though the processing and sale of cyclotron-produced isotopes were terminated, the Atomic Energy Commission continued to make its cyclotrons available for irradiation services under terms and conditions generally in effect

for use of other Atomic Energy Commission facilities. Accordingly, persons desiring the service may still have their targets irradiated by the Atomic Energy Commission to the extent that the Atomic Energy Commission's own requirements for cyclotron time permit. We understand that a second company now plans to supply arsenic 74 and proposes to have its material irradiated at Oak Ridge.

Based upon available information we believe that price rather than shortage of material has been a limiting factor in the use of the isotope. The 86-inch cyclotron at Oak Ridge has been undergoing modification for the past year and has only recently resumed operations. There has been some indication that if new techniques now being explored are successful, it may be possible to produce arsenic 74 at a substantially lower cost as an unprocessed target. These new techniques are still in the experimental stage, but if they are successful we would expect that any cost reductions resulting from them would be reflected in the prices charged by commercial suppliers who have their target irradiated in the Oak Ridge cyclotron.

To the extent that the present price of arsenic 74 is impeding its use, organizations desiring to purchase it for research purposes may solicit assistance, by way of applications for research contracts from various foundations, the Atomic Energy Commission, and possibly the United States Public Health Service. Normally this form of assistance is not available for isotopes used in routine clinical treatment.

Cobalt 60

With respect to cobalt 60 for teletherapy, the Commission has already taken measures to increase the available supply. In anticipation of increased demand for this isotope the Commission, in August 1955, authorized the production of approximately 200,000 curies of high specific activity cobalt 60 at Savannah River. This material is scheduled for discharge from the reactors during the next few weeks and should be more than adequate to meet all current requirements. Additional production to follow has been authorized.

Plans for meeting future needs for cobalt 60 have been under virtually continuous study within the Commission. Production at Savannah River will be continued at least until the end of this year. Meanwhile, both the expected future demand for cobalt 60 and available facilities for producing it will be further analyzed. The production cycle for teletherapy quality cobalt 60 is approximately 1 year and requirements must therefore be anticipated quite well in advance.

The amount of teletherapy quality cobalt 60 which can be produced depends upon the amount of high flux neutron irradiation space which can be made available for this purpose and still meet other important program needs. For example, the material can be and is being produced at Savannah River, but only by displacing production of a proportionate quantity of special nuclear and other materials for defense purposes. Thus the requirements for cobalt 60 must be weighed against requirements for these materials.

The Commission will continue, of course, to use its best efforts to provide adequate supplies of cobalt 60 until such time as private sources become available.

Sincerely yours,

K. E. FIELDS, *General Manager.*

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